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(54) Title: 3' GENOMIC PROMOTER REGION AND POLYMERASE GENE MUTATIONS RESPONSIBLE FOR ATTENUATION IN VIRUSES OF THE ORDER DESIGNATED MONONEGAVIRALES

(57) Abstract

Isolated, recombinantly-generated, attenuated, nonsegmented, negative-sense, single stranded RNA viruses of the Order Mononegavirales having at least one attenuating mutation in the 3' genomic promoter region and having at least one attenuating mutation in the RNA polymerase gene are described. Vaccines are formulated comprising such viruses and a physiologically acceptable carrier. The vaccines are used for immunizing an individual to induce protection against a nonsegmented, negative-sense, single stranded RNA virus of the Order Mononegavirales.

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3' GENOMIC PROMOTER REGION AND POLYMERASE GENE MUTATIONS RESPONSIBLE FOR ATTENUATION IN VIRUSES OF THE ORDER DESIGNATED MONONEGAVIRALES

Field Of The Invention

This invention relates to isolated, recombinantly-generated, attenuated, nonsegmented, negative-sense, single stranded RNA viruses of the Order designated Mononegavirales having at least one attenuating mutation in the 3' genomic promoter region and having at least one attenuating mutation in the RNA polymerase gene. This invention was made with Government support under a grant awarded by the Public Health Service. The Government has certain rights in the invention.

Background Of The Invention

Enveloped, negative-sense, single stranded RNA viruses are uniquely organized and expressed. The genomic RNA of negative-sense, single stranded viruses serves two template functions in the context of a nucleocapsid: as a template for the synthesis of messenger RNAs (mRNAs) and as a template for the synthesis of the antigenome (+) strand. Negative-sense, single stranded RNA viruses encode and package their own RNA dependent RNA Polymerase. Messenger RNAs are only synthesized once the virus has been uncoated in the infected cell. Viral replication occurs after synthesis of the mRNAs and requires the continuous synthesis of viral proteins. The newly synthesized antigenome (+) strand serves as the template for generating further copies of the (-) strand genomic RNA.

The polymerase complex actuates and achieves transcription and replication by engaging the cis-acting signals at the 3' end of the genome, in particular, the promoter region. Viral genes are then transcribed from the genome template unidirectionally from its 3' to its 5' end. There is always less mRNA made from the downstream genes (e.g., the polymerase gene (L)) relative to their upstream neighbors (i.e., the nucleoprotein gene (N)). Therefore, there is always a gradient of mRNA abundance according to the position of the genes relative to the 3'-end of the genome.

Based on the revised reclassification in 1993 by the International Committee on the Taxonomy of Viruses, an Order, designated Mononegavirales, has been established. This Order contains three families of enveloped viruses with single stranded, nonsegmented RNA genomes of minus polarity (negative-sense). These families are the Paramyxoviridae, Rhabdoviridae and Filoviridae. The family Paramyxoviridae has been further divided into two subfamilies, Paramyxovirinae and Pneumovirinae. The subfamily Paramyxovirinae contains three genera, *Paramyxovirus*, *Rubulavirus* and *Morbillivirus*. The subfamily Pneumovirinae contains the genus *Pneumovirus*.

The new classification is based upon morphological criteria, the organization of the viral genome, biological activities and the sequence relationships of the proteins. The morphological distinguishing feature among enveloped viruses for the subfamily Paramyxovirinae is the size and shape of the nucleocapsids (diameter 18mm, 1mm in length, pitch of 5.5 nm), which have a left-handed helical symmetry. The biological criteria are: 1) antigenic cross-reactivity between members of a genus, and 2) the presence of neuraminidase activity in the genera *Paramyxovirus*,

Rubulavirus and its absence in genus *Morbillivirus*. In addition, variations in the coding potential of the P gene are considered, as is the presence of an extra gene (SH) in Rubulaviruses.

Pneumoviruses can be distinguished from Paramyxovirinae morphologically because they contain narrow nucleocapsids. In addition, pneumoviruses have major differences in the number of protein-encoding cistrons (10 in pneumoviruses versus 6 in Paramyxovirinae) and an attachment protein (G) that is very different from that of Paramyxovirinae. Although the paramyxoviruses and pneumoviruses have six proteins that appear to correspond in function (N, P, M, G/H/HN, F and L), only the latter two proteins exhibit significant sequence relatedness between the two subfamilies. Several pneumoviral proteins lack counterparts in most of the paramyxoviruses, namely the nonstructural proteins NS1 and NS2, the small hydrophobic protein SH, and a second protein M2. Some paramyxoviral proteins, namely C and V, lack counterparts in pneumoviruses. However, the basic genomic organization of pneumoviruses and paramyxoviruses is the same. The same is true of rhabdoviruses and filoviruses. Table 1 presents the current taxonomical classification of these viruses, together with examples of each genus.

Table 1

Classification of Nonsegmented, negative-sense, single stranded RNA Viruses of the Order Mononegavirales

<u>Family Paramyxoviridae</u>

Subfamily Paramyxovirinae

Genus *Paramyxovirus*

Sendai virus (mouse parainfluenza virus type 1)

Human parainfluenza virus (PIV) types 1 and 3

Bovine parainfluenza virus (BPV) type 3

Genus *Rubulavirus*

Simian virus 5 (SV) (Canine parainfluenza virus type 2)

Mumps virus

Newcastle disease virus (NDV) (avian Paramyxovirus 1)

Human parainfluenza virus types 2, 4a and 4b

Genus *Morbillivirus*

Measles virus (MV)

Dolphin Morbillivirus

Canine distemper virus (CDV)

Peste-des-petits-ruminants virus

Phocine distemper virus

Rinderpest virus

Subfamily Pneumovirinae

Genus *Pneumovirus*

Human respiratory syncytial virus (RSV)

Bovine respiratory syncytial virus

Pneumonia virus of mice

Turkey rhinotracheitis virus

<u>Family Rhabdoviridae</u>

Genus *Lyssavirus*

Rabies virus

Genus *Vesiculovirus*

Vesicular stomatitis virus

Genus *Ephemerovirus*

Bovine ephemeral fever virus

<u>Family Filovirdae</u>

Genus *Filovirus*

Marburg virus

For many of these viruses, no vaccines of any kind are available. Thus, there is a need to develop vaccines against such human and animal pathogens. Such vaccines would have to elicit a protective immune response in the recipient. The qualitative and quantitative features of such a favorable response are extrapolated from those seen in survivors of natural virus infection, who, in general, are protected from reinfection by the same or highly related viruses for some significant duration thereafter.

A variety of approaches can be considered in seeking to develop such vaccines, including the use of: (1) purified individual viral protein vaccines (subunit vaccines); (2) inactivated whole virus preparations; and (3) live, attenuated viruses.

Subunit vaccines have the desirable feature of being pure, definable and relatively easily produced in abundance by various means, including recombinant DNA expression methods. To date, with the notable exception of hepatitis B surface antigen, viral subunit vaccines have generally only elicited short-lived and/or inadequate immunity, particularly in naive recipients.

Formalin inactivated whole virus preparations of polio (IPV) and hepatitis A have proven safe and efficacious. In contrast, immunization with similarly inactivated whole viruses such as respiratory syncytial virus and measles virus vaccines elicited unfavorable immune responses and/or response profiles which predisposed vaccinees to exaggerated or aberrant disease when subsequently confronted with the natural or "wild-type" virus.

Early attempts (1966) to vaccinate young children using a parenterally administered formalin-inactivated RSV vaccine. Unfortunately, several field

trials of this vaccine revealed serious adverse reactions -- the development of a severe illness with unusual features following subsequent natural infection with RSV (Bibliography entries 1,2). It has been suggested that this formalinized RSV antigen elicited an abnormal or unbalanced immune response profile, predisposing the vaccinee to RSV disease (3,4).

Thereafter, live, attenuated RSV vaccine candidates were generated by cold passage or chemical mutagenesis. These RSV strains were found to have reduced virulence in seropositive adults. Unfortunately, they proved either over or under-attenuated when given to seronegative infants; in some cases, they also were found to lack genetic stability (5,6). Another vaccination approach using parenteral administration of live virus was ineffective and efforts along this line were discontinued (7). Notably, these live RSV vaccines were never associated with disease enhancement as observed with the formalin-inactivated RSV vaccine described above. Currently, there are no RSV vaccines approved for administration to humans, although clinical trials are now in progress with cold-passaged, chemically mutagenized strains of RSV designated A2 and B-1.

Appropriately attenuated live derivatives of wild-type viruses offer a distinct advantage as vaccine candidates. As live, replicating agents, they initiate infection in recipients during which viral gene products are expressed, processed and presented in the context of the vaccinee's specific MHC class I and II molecules, eliciting humoral and cell-mediated immune responses, as well as the coordinate cytokine patterns, which parallel the protective immune profile of survivors of natural infection.

This favorable immune response pattern is contrasted with the delimited responses elicited by inactivated or subunit vaccines, which typically are largely restricted to the humoral immune surveillance arm. Further, the immune response profile elicited by some formalin inactivated whole virus vaccines, e.g., measles and respiratory syncytial virus vaccines developed in the 1960's, have not only failed to provide sustained protection, but in fact have led to a predisposition to aberrant, exaggerated, and even fatal illness, when the vaccine recipient later confronted the wild-type virus.

While live, attenuated viruses have highly desirable characteristics as vaccine candidates, they have proven to be difficult to develop. The crux of the difficulty lies in the need to isolate a derivative of the wild-type virus which has lost its disease-producing potential (i.e., virulence), while retaining sufficient replication competence to infect the recipient and elicit the desired immune response profile in adequate abundance.

Historically, this delicate balance between virulence and attenuation has been achieved by serial passage of a wild-type viral isolate through different host tissues or cells under varying growth conditions (such as temperature). This process presumably favors the growth of viral variants (mutants), some of which have the favorable characteristic of attenuation. Occasionally, further attenuation is achieved through chemical mutagenesis as well.

This propagation/passage scheme typically leads to the emergence of virus derivatives which are temperature sensitive, cold-adapted and/or altered in their host range -- one or all of which are changes

from the wild-type, disease-causing viruses -- i.e., changes that may be associated with attenuation.

Several live virus vaccines, including those for the prevention of measles and mumps (which are paramyxoviruses), and for protection against polio and rubella (which are positive strand RNA viruses), have been generated by this approach and provide the mainstay of current childhood immunization regimens throughout the world.

Nevertheless, this means for generating attenuated live virus vaccine candidates is lengthy and, at best, unpredictable, relying largely on the selective outgrowth of those randomly occurring genomic mutants with desirable attenuation characteristics. The resulting viruses may have the desired phenotype in *vitro*, and even appear to be attenuated in animal models. However, all too often they remain either under- or overattenuated in the human or animal host for whom they are intended as vaccine candidates.

Even as to current vaccines in use, there is still a need for more efficacious vaccines. For example, the current measles vaccines provide reasonably good protection. However, recent measles epidemics suggest deficiencies in the efficacy of current vaccines. Despite maternal immunization, high rates of acute measles infection have occurred in children under age one, reflecting the vaccines' inability to induce anti-measles antibody levels comparable to those developed following wild-type measles infection (8,9,10). As a result, vaccine-immunized mothers are less able to provide their infants with sufficient transplacentally-derived passive antibodies to protect the newborns beyond the first few months of life.

Acute measles infections in previously immunized adolescents and young adults point to an additional problem. These secondary vaccine failures indicate limitations in the current vaccines' ability to induce and maintain antiviral protection that is both abundant and long-lived (11,12,13). Recently, yet another potential problem was revealed. The hemagglutinin protein of wild-type measles isolated over the past 15 years has shown a progressively increasing distance from the vaccine strains (14). This "antigenic drift" raises legitimate concerns that the vaccine strains may not contain the ideal antigenic repertoire needed to provide optimal protection. Thus, there is a need for improved vaccines.

Rational vaccine design would be assisted by a better understanding of these viruses, in particular, by the identification of the virally encoded determinants of virulence as well as those genomic changes which are responsible for attenuation.

Summary Of The Invention

Accordingly, it is an object of this invention to identify those regions of the genome of the RNA viruses of the Order Mononegavirales where mutations result in attenuation of those viruses.

It is a further object of this invention to produce recombinantly-generated viruses which incorporate such attenuating mutations in their genomes.

It is still a further object of this invention to formulate vaccines containing such attenuated viruses.

These and other objects of the invention as discussed below are achieved by the generation and

isolation of recombinantly-generated, attenuated, nonsegmented, negative-sense, single stranded RNA viruses of the Order Mononegavirales having at least one attenuating mutation in the 3' genomic promoter region and having at least one attenuating mutation in the RNA polymerase gene.

In the case of measles virus, at least one attenuating mutation in the 3' genomic promoter region is selected from the group consisting of nucleotide 26 (A → T), nucleotide 42 (A → T or A → C) and nucleotide 96 (G → A), where these nucleotides, as well as others delineated in this application (unless stated otherwise), are presented in positive strand, antigenomic, that is, message (coding) sense, and at least one attenuating mutation in the RNA polymerase gene is selected from the group consisting of nucleotide changes which produce changes in an amino acid selected from the group consisting of residues 331 (isoleucine → threonine), 1409 (alanine → threonine), 1624 (threonine → alanine), 1649 (arginine → methionine), 1717 (aspartic acid → alanine), 1936 (histidine → tyrosine), 2074 (glutamine → arginine) and 2114 (arginine → lysine).

In the case of human parainfluenza virus type 3, at least one attenuating mutation in the 3' genomic promoter region is selected from the group consisting of nucleotide 23 (T → C), nucleotide 24 (C → T), nucleotide 28 (G → T) and nucleotide 45 (T → A), and at least one attenuating mutation in the RNA polymerase gene is selected from the group consisting of nucleotide changes which produce changes in an amino acid selected from the group consisting of residues 942 (tyrosine → histidine), 992 (leucine →

phenylalanine), 1292 (leucine → phenylalanine), and 1558 (threonine → isoleucine).

In the case of human respiratory syncytial virus subgroup B, at least one attenuating mutation in the 3' genomic promoter region is selected from the group consisting of nucleotide 4 (C → G) and the insertion of an additional A in the stretch of A's at nucleotides 6-11, and at least one attenuating mutation in the RNA polymerase gene is selected from the group consisting of nucleotide changes which produce changes in an amino acid selected from the group consisting of residues 353 (arginine → lysine), 451 (lysine → arginine), 1229 (aspartic acid → asparagine), 2029 (threonine → isoleucine) and 2050 (asparagine → aspartic acid).

In another embodiment of this invention, attenuated virus is used to prepare vaccines which elicit a protective immune response against the wild-type form of the virus.

In yet another embodiment of this invention, an isolated, positive strand, antigenomic message sense nucleic acid molecule (or an isolated, negative strand genomic sense nucleic acid molecule) having the complete viral nucleotide sequence (whether of wild-type virus or virus attenuated by non-recombinant means) is manipulated by introducing one or more of the attenuating mutations described in this application to generate an isolated, recombinantly-generated attenuated virus. This virus is then used to prepare vaccines which elicit a protective immune response against the wild-type form of the virus.

In still another embodiment of this invention, such a complete wild-type or vaccine viral nucleotide sequence is used: (1) to design PCR primers for use in a PCR assay to detect the presence of the

corresponding virus in a sample; or (2) to design and select peptides for use in an ELISA to detect the presence of the corresponding virus in a sample.

Brief Description Of The Figures

Figure 1 depicts the passage history of the Edmonston measles virus (15). The abbreviations have the following meanings: HK - human kidney; HA - human amnion; CE(am) - chick embryo; CEF - chick embryo fibroblast; DK - dog kidney; WI-38 - human diploid cells; SK - sheep kidney; * - plaque cloning. The number following each abbreviation represents the number of passages.

Figure 2 depicts a map of the measles virus genome showing putative cis-acting regulatory elements at and near the genome and antigenome termini. Top - a schematic map of the measles virus genome, beginning at the 3' end with 52 nucleotides of leader sequence (l) and ending at the 5' terminus with 37 nucleotides of trailer sequence (t). Gene boundaries are denoted by vertical bars; below each gene is the number of cistronic nucleotides. Bottom - an expanded schematic view of the 3' extended genomic promoter regions of genome and antigenome, showing the position and sequence of the two highly conserved domains, A and B. The intervening intergenic trinucleotide is denoted as well. Nascent 5' RNAs encompassing the A' to B' regions are presumed to contain the regulatory sequence at which the N protein encapsidation initiates.

Figure 3 depicts a genetic map of the RSV subgroup B wild-type strains designated 2B and 18537 (top portion), the intergenic sequences of those strains (middle portion) and the 68 nucleotide overlap between the M2 and L genes (bottom portion). The RSV

2B strain has six fewer nucleotides in the G gene, encoding two fewer amino acid residues in the G protein, as compared to the 18537 strain. The 2B strain has 145 nucleotides in the 5′ trailer region, as compared to 149 nucleotides in the 18537 strain. The 2B strain has one more nucleotide in each of the NS-1, NS-2 and N genes, and one fewer nucleotide in each of the M and F genes, as compared to the 18537 strain.

Detailed Description Of The Invention

Transcription and replication of negative-sense, single stranded RNA viral genomes are achieved through the enzymatic activity of a multimeric protein acting on the ribonucleoprotein core (nucleocapsid). Naked genomic RNA cannot serve as a template. Instead, these genomic sequences are recognized only when they are entirely encapsidated by the N protein into the nucleocapsid structure. It is only in that context that the genomic and antigenomic terminal promoter sequences are recognized to initiate the transcriptional or replication pathways.

All paramyxoviruses require the two viral proteins, L and P, for these polymerase pathways to proceed. The pneumoviruses, including RSV, also require the transcription elongation factor, M2, for the transcriptional pathway to proceed efficiently. Additional cofactors may also play a role, including perhaps the virus-encoded NS1 and NS2 proteins, as well as perhaps host-cell encoded proteins.

However, considerable evidence indicates that it is the L protein which performs most, if not all, the enzymatic processes associated with transcription and replication, including initiation, and termination of ribonucleotide polymerization, capping and

polyadenylation of mRNA transcripts, methylation and perhaps specific phosphorylation of P proteins. The L protein's central role in genomic transcription and replication is supported by its large size, sensitivity to mutations, and its catalytic level of abundance in the transcriptionally active viral complex (16).

These considerations led to the proposal that L proteins consist of a linear array of domains whose concatenated structure integrates discrete functions (17). Indeed, three such delimited, discrete elements within the negative-sense virus L protein have been identified based on their relatedness to defined functional domains of other well-characterized proteins. These include: (1) a putative RNA template recognition and/or phosphodiester bond formation domain; (2) an RNA binding element; and (3) an ATP binding domain. All prior studies of L proteins of nonsegmented negative-sense, single stranded RNA viruses have revealed these putative functional elements (17).

Without being bound by the following, it is reasonable to presume that these non-protein coding, promoter and other cis-acting genomic regulatory domains are important determinants of the efficiency with which transcription and replication by measles virus (MV) and other viruses of the Order Mononegavirales are actualized, in association with the L protein, and that they may therefore be virulence determinants for these viruses as well.

In summary, the invention is believed to encompass a coordinate set of changes between the cis-acting regulatory signal (3' genomic promoter region) and the polymerase gene (L) which results in attenuation of the virus while retaining sufficient ability of the virus to replicate. Attenuation is

optimized by rational mutations of the 3' genomic promoter region and the polymerase gene, which provide the desired balance of replication efficiency: so that the virus vaccine is no longer able to produce disease, yet retains its capacity to infect the vaccinee's cells, to express sufficiently abundant gene products to elicit the full spectrum and profile of desirable immune responses, and to reproduce and disseminate sufficiently to maximize the abundance of the immune response elicited.

Without being bound by the following, attenuating mutations in the extended promoter (3' genomic promoter region) and in the polymerase gene are believed to affect the display of cis-acting signals and the conformation of the polymerase complex engaging these signals. For example, when encapsidated, the promoter RNA is coiled in a helical array. Changes in promoter sequence may affect the relative positions at which the conserved signals are displayed relative to one another. Specifically, the measles wild-type 3' genomic promoter region has a pyrimidine (uracil) at positions 26 and 42 (the antigenomic message sense sequences have the purine adenine). The vaccine strains have purines at those positions (the antigenomic message sense sequences have the corresponding pyrimidines; see Table 3 in Example 1 below). The larger purines may change the distance and/or angular display between the conserved domains of the promoter (e.g, in measles, positions 1-11 and 87-98), resulting in an altered spatial presentation of the cis-acting signals to the polymerase.

Animal studies have demonstrated a decrease in viral replication sufficient to avoid illness but adequate to elicit the desired immune response. This likely represents a decrease in transcription, a

decrease in gene expression of virally encoded proteins, a decrease in antisense templates and, therefore, the production of fewer new genomes. The resulting attenuated viruses are significantly less virulent than the wild-type.

The attenuating mutations described herein may be introduced into viral strains by two methods:

(1) Conventional means such as chemical mutagenesis during virus growth in cell cultures to which a chemical mutagen has been added, selection of virus that has been subjected to passage at suboptimal temperature in order to select temperature sensitive and/or cold adapted mutations, identification of mutant virus that produce small plaques in cell culture, and passage through heterologous hosts to select for host range mutations. These viruses are then screened for attenuation of their biological activity in an animal model. Attenuated viruses are subjected to nucleotide sequencing of their 3' genomic promoter region and polymerase genes to locate the sites of attenuating mutations. Once this has been done, method (2) is then carried out.

(2) A preferred means of introducing attenuating mutations comprises making predetermined mutations using site-directed mutagenesis. These mutations are identified either by method (1) or by reference to closely-related viruses whose attenuating mutations are already known. One or more mutations are introduced into each of the 3' genomic promoter region and the polymerase gene. Cumulative effects of different combinations of coding and non-coding changes can also be assessed.

The mutations to the 3' genomic promoter region and polymerase gene are introduced by standard recombinant DNA methods into a DNA copy of the viral

genome. This may be a wild-type or a modified viral genome background (such as viruses modified by method (1)), thereby generating a new virus. Infectious clones or particles containing these attenuating mutations are generated using the cDNA "rescue" system, which has been applied to a variety of viruses, including Sendai virus (18); measles virus (19); respiratory syncytial virus (20); rabies (21); vesicular stomatitis virus (VSV) (15); and rinderpest virus (23); these references are hereby incorporated by reference. See, for measles virus rescue, published International patent application WO 97/06270, designating the United States (24); for PIV-3 rescue, U.S. provisional patent application 60/047575 (25); for RSV rescue, published International patent application WO 97/12032, designating the United States (26); these applications are hereby incorporated by reference.

Briefly, all Mononegavirales rescue systems can be summarized as follows: Each requires a cloned DNA equivalent of the entire viral genome placed between a suitable DNA-dependent RNA polymerase promoter (e.g., the T7 RNA polymerase promoter) and a self-cleaving ribozyme sequence (e.g., the hepatitis delta ribozyme) which is inserted into a propagatable bacterial plasmid. This transcription vector provides the readily manipulable DNA template from which the RNA polymerase (e.g., T7 RNA polymerase) can faithfully transcribe a single-stranded RNA copy of the viral antigenome (or genome) with the precise, or nearly precise, 5′ and 3′ termini. The orientation of the viral genomic DNA copy and the flanking promoter and ribozyme sequences determine whether antigenome or genome RNA equivalents are transcribed. Also required for rescue of new virus progeny are the virus-specific trans-acting proteins needed to encapsidate the naked,

single-stranded viral antigenome or genome RNA transcripts into functional nucleocapsid templates: the viral nucleocapsid (N or NP) protein, the polymerase-associated phosphoprotein (P) and the polymerase (L) protein. These proteins comprise the active viral RNA-dependent RNA polymerase which must engage this nucleocapsid template to achieve transcription and replication.

The trans-acting proteins required for measles virus rescue are the encapsidating protein N, and the polymerase complex proteins, P and L. For PIV-3, the encapsidating protein is designated NP, and the polymerase complex proteins are also referred to as P and L. For RSV, the virus-specific trans-acting proteins include N, P and L, plus an additional protein, M2, the RSV-encoded transcription elongation factor.

Typically, these viral trans-acting proteins are generated from one or more plasmid expression vectors encoding the required proteins, although some or all of the required trans-acting proteins may be produced within mammalian cells engineered to contain and express these virus-specific genes and gene products as stable transformants.

The typical (although not necessarily exclusive) circumstances for rescue include an appropriate mammallian cell milieu in which T7 polymerase is present to drive transcription of the antigenomic (or genomic) single-stranded RNA from the viral genomic cDNA-containing transcription vector. Either cotranscriptionally or shortly thereafter, this viral antigenome (or genome) RNA transcript is encapsidated into functional templates by the nucleocapsid protein and engaged by the required polymerase components produced concurrently from co-

transfected expression plasmids encoding the required virus-specific trans-acting proteins. These events and processes lead to the prerequisite transcription of viral mRNAs, the replication and amplification of new genomes and, thereby, the production of novel viral progeny, i.e., rescue.

For the rescue of rabies, VSV and Sendai, T7 polymerase is provided by recombinant vaccinia virus VTF7-3. This system, however, requires that the rescued virus be separated from the vaccinia virus by physical or biochemical means or by repeated passaging in cells or tissues that are not a good host for poxvirus. For MV cDNA rescue, this requirement is avoided by creating a cell line that expresses T7 polymerase, as well as viral N and P proteins. Rescue is achieved by transfecting the genome expression vector and the L gene expression vector into the helper cell line. Advantages of the host-range mutant of the vaccinia virus, MVA-T7, which expresses the T7 RNA polymerase, but does not replicate in mammalian cells, are exploited to rescue RSV, Rinderpest virus and MV. After simultaneous expression of the necessary encapsidating proteins, synthetic full length antigenomic viral RNA are encapsidated, replicated and transcribed by viral polymerase proteins and replicated genomes are packaged into infectious virions. In addition to such antigenomes, genome analogs have now been successfully rescued for Sendai and PIV-3 (25,27).

The rescue system thus provides a composition which comprises a transcription vector comprising an isolated nucleic acid molecule encoding a genome or antigenome of a nonsegmented, negative-sense, single stranded RNA virus of the Order Mononegavirales having at least one attenuating mutation in the 3' genomic promoter region and having at least one attenuating

mutation in the RNA polymerase gene, together with at least one expression vector which comprises at least one isolated nucleic acid molecule encoding the trans-acting proteins necessary for encapsidation, transcription and replication (e.g., N, P and L for measles virus; NP, P and L for PIV-3; N, P, L and M2 for RSV). Host cells are then transformed or transfected with the at least two expression vectors just described. The host cells are cultured under conditions which permit the co-expression of these vectors so as to produce the infectious attenuated virus.

The rescued infectious virus is then tested for its desired phenotype (temperature sensitivity, cold adaptation, plaque morphology, and transcription and replication attenuation), first by *in vitro* means. The mutations at the cis-acting 3' genomic promoter region are also tested using the minireplicon system where the required trans-acting encapsidation and polymerase activities are provided by wild-type or vaccine helper viruses, or by plasmids expressing the N, P and different L genes harboring gene-specific attenuating mutations (19,28).

If the attenuated phenotype of the rescued virus is present, challenge experiments are conducted with an appropriate animal model. Non-human primates provide the preferred animal model for the pathogenesis of human disease. These primates are first immunized with the attenuated, recombinantly-generated virus, then challenged with the wild-type form of the virus. Monkeys are infected by various routes, including but not limited to intranasal, intratracheal or subcutaneous routes of inoculation (29). Experimentally infected rhesus and cynomolgus macaques have also served as animal models for studies of

vaccine-induced protection against measles (30). Protection is measured by such criteria as disease signs and symptoms, survival, virus shedding and antibody titers. If the desired criteria are met, the attenuated, recombinantly-generated virus is considered a viable vaccine candidate for testing in humans. The "rescued" virus is considered to be "recombinantly-generated", as are the progeny and later generations of the virus, which also incorporate the attenuating mutations.

Even if a "rescued virus is underattenuated or overattenuated relative to optimum levels for vaccine use, this is information which is valuable for developing such optimum strains.

Optimally, a codon containing an attenuating point mutation may be stabilized by introducing a second or a second plus a third mutation in the codon without changing the amino acid encoded by the codon bearing only the attenuating point mutation. Infectious virus clones containing the attenuating and stabilizing mutations are also generated using the cDNA "rescue" system described above.

Measles virus serves as a useful model for this invention, because sequence data are now available as described herein for the disease-causing wild-type virus and for the disease-preventing vaccines which have a demonstrated history of efficacy.

Measles virus was first isolated in tissue culture in 1954 (31) from an infected patient named David Edmonston. This Edmonston strain of measles became the progenitor for many live-attenuated measles vaccines including Moraten, which is the current vaccine in the United States (Attenuvax™; Merck Sharp & Dohme, West Point, PA) and was licensed in 1968 and has proven to be efficacious.

Aggressive immunization programs instituted in the mid to late 1960s resulted in the precipitous drop in reported measles cases from near 700,000 in 1965 to 1500 in 1983. In parallel, other vaccine strains were also developed from the Edmonston strain (see Fig. 1), Schwarz (Institut Merieux, Lyon, France), Zagreb (Zagreb, Yugoslavia) and AIK-C (Japan). These other vaccines have also proven to be efficacious and have been used extensively. An early, reactogenic, underattenuated vaccine strain (Rubeovax™: Merck Sharp & Dohme) produced measles-like illness in children and its use thus was discontinued. It, however, was further attenuated successfully to produce the Moraten vaccine strain (see Fig. 1) (32). Live measles virus vaccine provides a success story of the development of an efficacious vaccine and provides a model for understanding the molecular mechanisms of viral vaccine attenuation among nonsegmented, negative-sense, single stranded RNA viruses.

Because of its significance as a major cause of human morbidity and mortality, measles virus (MV) has been quite extensively studied. MV is a large, relatively spherical, enveloped particle composed of two compartments, a lipoprotein membrane and a ribonucleoprotein particle core, each having distinct biological functions (33). The virion envelope is a host cell-derived plasma membrane modified by three virus-specified proteins: The hemagglutinin (H; approximately 80 kilodaltons (kD)) and fusion ($F_{1,2}$; approximately 60 kD) glycoproteins project on the virion surface and confer host cell attachment and entry capacities to the viral particle (16). Antibodies to H and/or F are considered protective since they neutralize the virus' ability to initiate infection (34,35,36). The matrix (M; approximately 37

kD) protein is the amphipathic protein lining the membrane's inner surface, which is thought to orchestrate virion morphogenesis and thus consummate virus reproduction (37). The virion core contains the 15,894 nucleotide long genomic RNA upon which template activity is conferred by its intimate association with approximately 2600 molecules of the approximately 60 kD nucleocapsid (N) protein (38,39,40). Loosely associated with this approximately one micron long helical ribonucleoprotein particle are enzymatic levels of the viral RNA dependent RNA polymerase (L; approximately 240 kD) which in concert with the polymerase cofactor (P; approximately 70 kD), and perhaps yet other virus-specified as well as host-encoded proteins, transcribes and replicates the MV genome sequences (41).

To date, the entire nucleotide sequences (only for the Edmonston B laboratory strain and the AIK-C vaccine strain), coding potential, and organization of the MV genome have been reported (33). The six virion structural proteins are encoded by six contiguous, non-overlapping genes which are arrayed as follows: 3'-N-P-M-F-H-L-5'. Two additional MV gene products of as yet uncertain function have also been identified. These two nonstructural proteins, known as C (approximately 20 kD) and V (approximately 45 kD), are both encoded by the P gene, the former by a second reading frame within the P mRNA; the latter by a cotranscriptionally edited P gene-derived mRNA which encodes a hybrid protein having the amino terminal sequences of P and a new zinc finger-like cysteine-rich carboxy terminal domain (16).

In addition to the sequences encoding the virus-specified proteins, the MV genome contains distinctive non-protein coding domains resembling those

directing the transcriptional and replicative pathways of related viruses (16,42). These regulatory signals lie at the 3' and 5' ends of the MV genome and in short internal regions spanning each intercistronic boundary. The former encode the putative promoter and/or regulatory sequence elements directing genomic transcription, genome and antigenome encapsidation, and replication. The latter signal transcription termination and polyadenylation of each monocistronic viral mRNA and then reinitiation of transcription of the next gene. In general, the MV polymerase complex appears to respond to these signals much as the RNA-dependent RNA polymerases of other non-segmented negative strand RNA viruses (16,42,43,44).

Transcription initiates at or near the 3' end of the MV genome and then proceeds in a 5' direction producing monocistronic mRNAs (40,42,45). As the polymerase traverses the MV genomic template, it encounters putative stop/start signals which, in 3' to 5' order, are: a semi-conserved transcription termination/polyadenylation signal (A/G U/C UA A/U NN A_4, where N may be any of the four bases) at which each monocistronic RNA is completed; a non-transcribed intergenic trinucleotide punctuation mark (CUU; except at the H:L boundary where it is CGU); and a semiconserved start signal for transcription initiation of the next gene (AGG A/G NN C/A A A/G G A/U, where N may be any of the four bases) (45,46). Since some polymerase complexes fail to reinitiate, the abundance of each MV mRNA diminishes in parallel with the distance of the encoding gene from the genomic 3' end. This mRNA gradient directly corresponds to the relative abundance of each virus-specified protein. This indicates that MV protein expression is ultimately controlled at the transcriptional level (44).

The 3' and 5' MV genomic termini contain non-protein coding sequences with distinct parallels to the leader and trailer RNA encoding regions of VSV (42). Nucleotides 1-55 define the region between the genomic 3' terminus and the beginning of the N gene, while 37 additional nucleotides can be found between the end of the L gene and the 5' terminus of the genome. However, unlike VSV, or even the paramyxoviruses Sendai and NDV, MV does not transcribe these terminal regions into short, unmodified (+) or (-) sense leader RNAs (47,48,49). Instead, leader readthrough transcripts, including full-length polyadenylated leader:N, leader:N:P, leader:N:P:M, and of course full-length antigenome MV RNAs are transcribed (48,49). Thus, the short leader transcript, the key operational element determining the switch from transcription to replication of the VSV single-stranded, negative polarity genome (50,51,52), seems absent in MV. This leads to consideration and exploration of alternative models for this crucial reproductive event (42).

Measles virus, as well as all other Mononegavirales except the rhabdoviruses, appears to have extended its terminal regulatory domains beyond the confines of leader and trailer encoding sequences (42). For measles, these regions encompass the 107 3' genomic nucleotides (the "3' genomic promoter region", also referred to as the "extended promoter", which comprises 52 nucleotides encoding the leader region, followed by three intergenic nucleotides, and 52 nucleotides encoding the 5' untranslated region of N mRNA) and the 109 5' end nucleotides (69 encoding the 3' untranslated region of L mRNA, the intergenic trinucleotide and 37 nucleotides encoding the trailer). Within these 3' terminal approximately 100 nucleotides

of both the genome and antigenome are two short regions of shared nucleotide sequence: 14 of 16 nucleotides at the absolute 3' ends of the genome and antigenome are identical. Internal to those termini, an additional region of 12 nucleotides of absolute sequence identity have been located. Their position at and near the sites at which the transcription of the MV genome must initiate and replication of the antigenome must begin, suggests that these short unique sequence domains encompass an extended promoter region.

These discrete sequence elements may dictate alternative sites of transcription initiation -- the internal domain mandating transcription initiation at the N gene start site, and the 3' terminal domain directing antigenome production (42,48,53). In addition to their regulatory role as cis-acting determinants of transcription and replication, these 3' extended genomic and antigenomic promoter regions encode the nascent 5' ends of antigenome and genome RNAs, respectively. Within these nascent RNAs reside as yet unidentified signals for N protein nucleation, another key regulatory element required for nucleocapsid template formation and consequently for amplification of transcription and replication. Figure 2 schematically shows the location and sequence of these highly conserved, putative cis-acting regulatory domains.

Terminal non-protein coding regions similar in location, size and spacing are present in the genomes of other members of the genus *Paramyxoviridae*, though only 8-11 of their absolute terminal nucleotides are shared by MV (42,54). The genomic terminii of the *Morbillivirus* canine distemper virus (CDV) displays a greater degree of homology with its MV relative: 73% of the nucleotides of the leader and trailer sequences

of these two viruses are identical, including 16 of 18 at the absolute 3' termini and 17 of 18 at their 5' ends (55). No accessory internal CDV genomic domain-sharing homology to that of the MV extended promoter has been found. However, there is a 20 nucleotide long stretch lying between CDV genomic nucleotides 85 and 104 and 15,587 and 15,606 in which 15 of the 20 nucleotides are complementary (Gene Bank accession number AF 14953). This indicates that CDV, like MV contains an additional region within its non-coding 3' genomic and antigenomic ends that may provide important cis-acting promoter and/or regulatory signals (55).

Additionally, the precise length of the 3'-leader region (55 nucleotides) is identical among several members of the Family Paramyxoviridae (MV, CDV, PIV-3, BPV-3, SV and NDV). Further evidence for the importance of these extended, non-protein coding regions comes from analyses of a large number of distinct copy-back Defective Interfering Viruses (DIs) recently cloned from subacute sclerosing panencephalitis (SSPE) brain tissue. No DI with a stem shorter than the 95 5' terminal genomic nucleotides was found. This indicates that the minimal signals needed for MV DI RNA replication and encapsidation extend well beyond the 37 nucleotide long trailer sequence to encompass the additional internal putative regulatory domain (56).

As exemplified in part by measles virus, this invention is directed to the concept that important virulence/attenuation determinants reside in viral genomic non-protein coding regulatory regions and in the transacting transcription/replication enzyme complex with which these cis-acting elements must interact. The cis-acting domains are found both at the 3' and 5' ends of the MV genome, flanking the six

contiguous genes encoding viral structural proteins; and within the MV genome as short regions encompassing internal intergenic boundaries. The former encode the putative promoter and/or regulatory sequence elements directing the vital processes of genomic transcription, genome and antigenome encapsidation, and replication. The latter signal transcription termination and polyadenylation of each monocistronic viral mRNA and then reinitiation of transcription of the next gene. The transcription/replication enzyme, RNA dependent RNA polymerase molecule can modulate transcription and/or replicative efficiency, thereby determining the abundance of cytopathic viral gene products and/or virion progeny.

Proof of the concept of this invention for measles virus is obtained by first determining the nucleotide sequences of the non-coding regulatory regions (3' genomic promoter region) and the coding regions of the L gene (with predicted amino acid sequences) of the progenitor Edmonston wild-type MV isolate, together with available measles vaccine strains derived from this isolate (see Figure 1). Independent other wild-type isolates were examined for comparative purposes as well.

The nucleotide sequences (in positive strand, antigenomic, message sense) of four wild-type and five vaccine measles strains, as well as the deduced amino acid sequences of the RNA polymerase (L protein) of these measles viruses, are set forth as follows with reference to the appropriate SEQ ID NOS. contained herein:

Virus	Nucleotide Sequence	L Protein Sequence
Wild-Type		
Edmonston	SEQ ID NO:1	SEQ ID NO:2
1977	SEQ ID NO:3	SEQ ID NO:4
1983	SEQ ID NO:5	SEQ ID NO:6
Montefiore	SEQ ID NO:7	SEQ ID NO:8
Vaccine		
Rubeovax™	SEQ ID NO:9	SEQ ID NO:10
Moraten	SEQ ID NO:11	SEQ ID NO:12
Zagreb	SEQ ID NO:13	SEQ ID NO:14
AIK-C	SEQ ID NO:15	SEQ ID NO:16

Each measles virus genome listed above is 15,894 nucleotides in length. Translation of the L gene starts with the codon at nucleotides 9234-9236; the translation stop codon is at nucleotides 15783-15785. The translated L protein is 2,183 amino acids long.

Note that nucleotide 2499 of 1983 wild-type measles virus is indicated as "G" in SEQ ID NO:5. In fact, the base is actually a mixture of "G" and "C". Also note that nucleotide 2143 of Rubeovax™ vaccine virus is indicated as "T" in SEQ ID NO:9. In nine clones sequenced, this base was "T" in seven and "C" in two; thus, this base can be "T" or "C".

In addition, the Schwarz vaccine virus genome is identical to that of the Moraten vaccine virus genome (SEQ ID NO:11), except that at nucleotides 4917 and 4924, Schwarz has a "C" instead of a "T".

Nucleotide differences distinguishing the 3' genomic promoter region and nucleotide and amino acid differences distinguishing the L gene and L protein sequences of the Edmonston wild-type isolate, vaccine strains and other independently isolated wild-type

viruses were then compared and aligned (see Tables 3-5 in Example 1 below).

As shown in Table 3, there were three mutations from the 3' genomic promoter region (in antigenomic, message sense) of the progenitor wild-type MV isolate and the derivative vaccine strains: At nucleotide position 26, from "A" to "T"; at position 42, from "A" to "C" or from "A" to "T"; and in the case of Zagreb only, at position 96, from "G" to "A". In addition, the other examined wild-type isolates differed from both the progenitor wild-type isolate and the vaccine strains at position 50 by having "A" instead of "G".

The predicted amino acid sequences of the L genes of measles vaccine strains (Rubeovax™, Moraten, Schwarz, AIK-C and Zagreb) and wild-type isolates (1977, 1983 and Montefiore), differ from the progenitor strain (Edmonston) at 49 positions in the 2183 amino acid long open reading frame (see Tables 4 and 5 in Example 1 below).

These amino acid differences can be divided into four categories:

(1) Positions where one vaccine strain differs from the progenitor, as well as from other vaccine and wild-type strains, suggesting a potential attenuation site.

(2) Specific differences between all wild-type and all vaccine sequences; these may also constitute important attenuation sites.

3) Residues where chronologically newer wild-types differ from older wild-types; which may be attributable to genetic drift.

(4) Positions where one or more vaccine strains and/or wild-type strains have common amino acids and differ from all the other strains; these

changes may represent lineage-specific, potentially attenuating changes within the vaccine strains and relatedness among the wild-type isolates, respectively.

There were four category (1) changes where one vaccine differed from the other vaccines, as well as the wild-type strains. Two of these were in Moraten and Schwarz (amino acids 331 and 2114) and two were in AIK-C (1624 and 2074). These mutations are of special interest because all of these viruses are good vaccines. Thus, these positions are sites for attenuation.

Only one position, 1717, fits into category (2), with all wild-types having aspartic acid and all vaccines having alanine. Interestingly, this position is in one of two areas where the L genes of measles and canine distemper virus (which are otherwise highly homologous) do not show exceptional conservation. This difference makes it more likely that 1717 is a key position for an attenuating mutation in measles.

There were five positions, 149, 636, 720, 2017 and 2119, where both chronologically newer wild-types (1983 and Montefiore) differ from older wild-types (Edmonston and 1977), which therefore fit into category (3). These differences suggest genetic drift rather than denoting sites of attenuating mutations. Not included in this total are 16 positions where Montefiore (the 1989 isolate) differed from the rest (see Table 5). These could be either genetic drift (category (3)) or random change (category (4)). The remaining 23 positions are category (4), with one or more of the viruses differing from the consensus.

Three of these positions (1409, 1649, 1936) are potentially attenuating category (4) mutations. These are changes where two vaccine strains have a common change from the progenitor wild-type strain.

These changes may be connected with the vaccine lineage leading to the Rubeovax™ and Moraten vaccines (Figure 1).

Applicants have found that their AIK-C vaccine strain nucleotide sequence differs from the published sequence (33) at 21 positions, including one insertion and one deletion. Several of these differences result in coding changes including two in the L gene (at amino acids 1477 and 2008).

Thus, the additional changes accrued within the L gene sequence as the measles progenitor strain is progressively attenuated to achieve a replicative capacity optimized for live vaccine purposes appears to be constrained and delimited. Presumably, this limited tolerance in the number and location of L gene changes is imposed not only by the need to preserve the multifunctional capacities of the polymerase, but also by the preexisting 3′ promoter changes with which the evolving L protein must interact to achieve transcription and replication. In other words, optimal virus attenuation requires coordinate (i.e., linked) changes in the polymerase protein and the cis-acting regulatory elements on which it acts.

The 3'-leader displays the least tolerance for change, allowing highly selected changes during the attenuation process at nucleotide position 26 (always the change of from "A" to "T"), and at position 42 (the change of from "A" to "C" or from "A" to "T") (in antigenomic, message sense). In the case of Zagreb only, there is a single further change, from "G" to "A" at position 96, which may be important when combined with Zagreb L gene-specific changes. The 3'-leader region seems to have undergone only one instance of genetic drift since 1954, with a change of "G" to "A" at position 50 (see Table 3).

The net change in the 3' genomic promoter region during the attenuation process is the replacement of two pyrimidines by two purines in genomic sense in all MV vaccine strains. The co-evolution of the L gene during these attenuation processes is believed to reflect selection of subtle changes favoring reproduction of the viruses in different host cells. All the vaccine strains were grown in chick embryo (CE) or chick embryo fibroblast (CEF) cells during their attenuation process (Figure 1). In addition, some vaccine strains have been exposed to unique host cells; i.e., Zagreb vaccine was grown in dog kidney cells and human diploid cells, while the AIK-C vaccine was adapted to sheep kidney cells. Moraten and Rubeovax™ were exclusively developed in CE and CEF.

Some of the lineage-specific L gene changes (position 1649 in Rubeovax™, Moraten and Schwarz vaccines and the change at position 1717 in all vaccines) represent a subset of adaptations of the L gene to the 3'-leader to modulate the transcription/replication processes for vaccine attenuation. Additionally, individual vaccine-specific changes (category (1)) may provide additional fine tune modulation of virus replication/transcription for each vaccine strain.

Based on Table 3 and the foregoing discussion, the key attenuating mutations for the MV 3' genomic promoter region are nucleotide 26 (A $\rightarrow$ T), nucleotide 42 (A $\rightarrow$ T or A $\rightarrow$ C) and nucleotide 96 (G $\rightarrow$ A) (in antigenomic, message sense).

Based on Table 4 and the foregoing discussion, the key attenuating sites for the L protein are as follows: amino acid residues 331 (isoleucine $\rightarrow$ threonine), 1409 (alanine $\rightarrow$ threonine), 1624

(threonine → alanine), 1649 (arginine → methionine), 1717 (aspartic acid → alanine), 1936 (histidine → tyrosine), 2074 (glutamine → arginine) and 2114 (arginine → lysine). It is understood that the nucleotide changes responsible for these amino acid changes are not limited to those set forth in Table 4 of Example 1 below; all changes in nucleotides which result in codons which are translated into these amino acids are within the scope of this invention.

Human parainfluenza virus type 3 (HPIV-3) is another nonsegmented, negative-sense, single stranded enveloped RNA virus. HPIV-3 belongs to the Family Paramyxoviridae (see Table 1). The genome of HPIV-3 is 15,462 nucleotides long and encodes six non-overlapping protein-encoding genes (57). Five of the genes encode a single virion structural protein each, which are designated NP (corresponding to the N protein of MV), M, F, HN (hemagglutinin-neuraminidase) and L. The sixth mRNA encodes the P protein, and by an overlapping 5' proximal open reading frame (ORF) encodes the C protein, and by the RNA editing mechanism, also encodes the D protein.

Like MV, HPIV-3 consists of a 3'-nonprotein coding leader region of 55 nucleotides, but unlike measles (where it is 37 nucleotides), it has a 44 nucleotide long 5'-trailer region. The polymerase transcribes the genome in a linear, sequential, start-stop manner which is guided by transcription signals in the RNA template.

Attempts to develop a live attenuated HPIV-3 vaccine by passaging the wild-type virus JS strain through cell culture at sub-optimal temperature has produced promising results (7,57). Several "cold passage" (cp) mutants were isolated for evaluation from different passage levels of the JS strain. One such

mutant resulted from 45 serial passages and was designated cp45.

This virus exhibited three interesting properties: (1) cold adaptation (*ca*): the ability to replicate efficiently at the suboptimal temperature of 20°C; (2) temperature sensitivity (*ts*): inability to replicate *in vitro* at temperatures greater than or equal to 39°C; and (3) small plaque morphology. This mutant appeared to be a promising vaccine candidate because: (a) its *ca*, *ts* and small plaque phenotype is stable after passage in cell culture; (b) its replication is restricted in both the upper and lower respiratory tract of hamsters; and (c) it induced significant protection in hamsters against subsequent challenge with wild-type HPIV-3 (58,59).

Evaluation of this strain in the rhesus monkey showed the attenuation mutations in cp45 to be a combination of *ts* and non-*ts* mutations (60). Subsequent evaluation in chimpanzees indicated that cp45 appeared to be satisfactorily attenuated while still able to induce a high level of protection against wild-type virus challenge (61). Later preliminary clinical evaluation of cp45 in seronegative human infants and small children suggested that this candidate vaccine strain is suitably infectious and attenuated, as well as being moderately immunogenic (61).

The cp45 strain has been grown in both fetal rhesus lung (FRhL) and Vero cells as follows: The PIV-3 cp45 virus grown in FRhL cells was prepared by inoculating confluent FRhL cell monolayers in tissue culture flasks at an MOI 0.1-1.0. The infected cell cultures were fed with EMEM medium and incubated at 32°C. About seven days later, when maximal cytopathic effects (syncytia) were observed, the virus was

harvested by subjecting the cultures to one freeze-thaw cycle, pooling the fluids and then storing the virus at -70 °C.

The PIV-3 cp45 virus grown in Vero cells was prepared by inoculating with virus a bioreactor culture of confluent monolayers of Vero cells on microcarrier beads which was continuously stirred. The infected bioreactor culture was maintained at 30°C. The virus was harvested 4-5 days later when syncytial CPE was observed. The culture fluid containing the virus was stored at -70 °C.

The nucleotide sequences (in positive strand, antigenomic, message sense) of the HPIV-3 JS wild-type strain (89) and the cp45 vaccine strain grown in FRhL and Vero cells, as well as the deduced amino acid sequences of the RNA polymerase (L protein) of these HPIV-3 viruses, are set forth as follows with reference to the appropriate SEQ ID NOS. contained herein:

Virus	Nucleotide Sequence	L Protein Sequence
Wild-Type		
JS	SEQ ID NO:17	SEQ ID NO:18
Vaccine		
FRhL cp45	SEQ ID NO:19	SEQ ID NO:20
Vero cp45	SEQ ID NO:21	SEQ ID NO:22

Each PIV-3 virus genome listed above is 15,462 nucleotides in length. Translation of the L gene starts with the codon at nucleotides 8646-8648; the translation stop codon is at nucleotides 15345-15347. The translated L protein is 2,233 amino acids long.

As detailed in Example 2 and Table 6 therein below, based upon the differences between the wild-type

JS strain and the FRhL-grown cp 45 mutant vaccine strain, the key attenuating mutations for the HPIV-3 3' genomic promoter region are nucleotide 23 ($T \rightarrow C$), nucleotide 24 ($C \rightarrow T$), nucleotide 28 ($G \rightarrow T$) and nucleotide 45 ($T \rightarrow A$) (in antigenomic, message sense). As also detailed in Example 2 and Table 6 therein below, key attenuating sites for the L protein of HPIV-3 include the following: amino acid residues 942 (tyrosine $\rightarrow$ histidine), 992 (leucine $\rightarrow$ phenylalanine) and 1558 (threonine $\rightarrow$ isoleucine).

In addition, the Vero-grown cp45 mutant vaccine strain contains an additional mutation resulting from a coding change in the L gene at amino acid residue 1292 (leucine $\rightarrow$ phenylalanine).

It is understood that the nucleotide changes responsible for these amino acid changes are not limited to those set forth in Example 2 below; all changes in nucleotides which result in codons which are translated into these amino acids are within the scope of this invention.

Human respiratory syncytial virus (RSV) is yet another nonsegmented, negative-sense, single stranded enveloped RNA virus. RSV belongs to the Subfamily Pneumovirinae and the genus *Pneumovirus* (see Table 1).

Two major subgroups of human RSV, designated A and B, have been identified based on reactivities of the F and G surface glycoproteins with monoclonal antibodies (62). More recently, the A and B lineages of RSV strains have been confirmed by sequence analysis (63,64). Bovine, ovine, and caprine strains of this virus have also been isolated. The host specificity of the virus is most clearly associated with the G attachment protein, which is highly divergent between

the human and the bovine/ovine strains (65,66), and may be influenced, at least in part, by receptor binding.

RSV is the primary cause of serious viral pneumonia and bronchiolitis in infants and young children. Serious disease, i.e., lower respiratory tract disease (LRD), is most prevalent in infants less than six months of age. It most commonly occurs in the nonimmune infant's first exposure to RSV. RSV additionally is associated with asthma and hyperreactive airways and it is a significant cause of mortality in "high risk" children with bronchopulmonary dysplasia and congenital heart disease (CHD). It is also one of the common viral respiratory infections predisposing to otitis media in children. In adults, RSV generally presents as uncomplicated upper respiratory illness; however, in the elderly it rivals influenza as a predisposing factor in the development of serious LRD, particularly bacterial bronchitis and pneumonia. Disease is always confined to the respiratory tract, except in the severely immunocompromised, where dissemination to other organs can occur. Virus is spread to others by fomites contaminated with virus-containing respiratory secretions, and infection initiates through the nasal, oral, or conjunctival mucosa.

RSV disease is seasonal and virus is usually isolated only in the winter months, e.g., from November to April in northern latitudes. The virus is ubiquitous, and over 90% of children have been infected at least once by 2 years of age. Multiple strains cocirculate. There is no direct evidence of antigenic drift (such as that seen with influenza A viruses), but sequence studies demonstrating accumulation of amino acid changes in the hypervariable regions of the G

protein and SH proteins suggest that immune pressure may drive virus evolution.

In mouse and cotton rat models, both the F and G proteins of RSV elicit neutralizing antibodies and immunization with these proteins alone provides longterm protection against reinfection (67,68).

In humans, complete immunity to RSV does not develop and reinfections occur throughout life (69,70); however, there is evidence that immune factors will protect against severe disease. A decrease in severity of disease is associated with two or more prior infections and there is evidence that children infected with one of the two major RSV subgroups may be somewhat protected against reinfection with the homologous subgroup (71), observations which suggest that a live attenuated virus vaccine may provide protection sufficient to prevent serious morbidity and mortality. Infection with RSV elicits both antibody and cell mediated immunity. Serum neutralizing antibody to the F and G proteins has been associated, in some studies, with protection from LRD, although reduction in upper respiratory disease (URD) has not been demonstrated. High levels of serum antibody in infants is associated with protection against LRD, and adminstration of intravenous immunoglobulin with high RSV neutralizing antibody titers has been shown to protect against severe disease in high risk children (70,72,73). The role of local immunity, and nasal antibody in particular, is being investigated.

The RSV virion consists of a ribonucleoprotein core contained within a lipoprotein envelope. The virions of pneumoviruses are similar in size and shape to those of all other paramyxoviruses. When visualized by negative staining and electron microscopy, virions are irregular in shape and range in

diameter from 150-300 nm (74). The nucleocapsid of this virus is a symmetrical helix similar to that of other paramyxoviruses, except that the helical diameter is 12-15 nm rather than 18nm. The envelope consists of a lipid bilayer that is derived from the host membrane and contains virally coded transmembrane surface glycoproteins. The viral glycoproteins mediate attachment and penetration and are organized separately into virion spikes. All members of paramyxovirus subfamily have hemagglutinating activity, but this function is not a defining feature for pneumoviruses, being absent in RSV but present in PVM (75). Neuraminidase activity is present in members of the genera Paramyxovirus, Rubulavirus, and is absent in Morbillivirus and Pneumovirus of mice (PVM) (75).

RSV possesses two subgroups, designated A and B. The wild-type RSV (strain 2B) genome is a single strand of negative-sense RNA of 15,218 nucleotides (SEQ ID NO:23) that are transcribed into ten major subgenomic mRNAs. Each of the ten mRNAs encodes a major polypeptide chain: Three are transmembrane surface proteins (G, F and SH); three are the proteins associated with genomic RNA to form the viral nucleocapsid (N, P and L); two are nonstructural proteins (NS1 and NS2) which accumulate in the infected cells but are also present in the virion in trace amounts and may play a role in regulating transcription and replication; one is the nonglycosylated virion matrix protein (M); and the last is M2, another nonglycosylated protein recently shown to be an RSV-specified transcription elongation factor (see Figure 3). These ten viral proteins account for nearly all of the viral coding capacity.

The viral genome is encapsidated with the major nucleocapsid protein (N), and is associated with

the phosphoprotein (P), and the large (L) polymerase protein. These three proteins have been shown to be necessary and sufficient for directing RNA replication of cDNA encoded RSV minigenomes (76). Further studies have shown that for transcription to proceed with full processing, the M2 protein (ORF 1) is required (74). When the M2 protein is missing, truncated transcripts predominate, and rescue of the full length genome does not occur (74).

Both the M (matrix protein) and the M2 proteins are internal virion-associated proteins that are not present in the nucleocapsid structure. By analogy with other nonsegmented negative-stranded RNA viruses, the M protein is thought to render the nucleocapsid transcriptionally inactive before packaging and to mediate its association with the viral envelope. The NS1 and NS2 proteins have only been detected in very small amounts in purified virions, and at this time are considered non-structural. Their functions are uncertain, though they may be regulators of transcription and replication. Three transmembrane surface glycoproteins are present in virions: G, F, and SH. G and F (fusion) are envelope glycoproteins that are known to mediate attachment and penetration of the virus into the host cell. In addition, these glycoproteins represent major independent immunogens (77). The function of the SH protein is unknown, although a recent report has implicated its involvement in the fusion function of the virus (78).

The genomes of two wild-type RSV subgroup B strains (2B and 18537) have now been sequenced in their entirety (see SEQ ID NOS:23 and 25, discussed below). Genomic RNA is neither capped nor polyadenylated (79). In both the virion and intracellularly, genomic RNA is tightly associated with the N protein.

The 3' end of the genomic RNA consists of a 44-nucleotide extragenic leader region that is presumed to contain the major viral promoter (Fig. 3). The 3' genomic promoter region is followed by ten viral genes in the order 3'-NS1-NS2-N-P-M-SH-G-F-M2-L-5' (Fig. 3). The L gene is followed by a 145-149 nucleotide extragenic trailer region (see Figure 3). Each gene begins with a conserved nine-nucleotide gene start signal 3'-GGGGCAAAU (except for the ten-nucleotide gene start signal of the L gene, which is 3'-GGG<u>A</u>CAAA<u>A</u>U; differences underlined). For each gene, transcription begins at the first nucleotide of the signal. Each gene terminates with a semi-conserved 12-14 nucleotide gene end (3'-A G U/G U/A ANNN U/A A_{3-5}) (where N can be any of the four bases) that directs transcription termination and polyadenylation (Fig. 3). The first nine genes are non-overlapping and are separated by intergenic regions that range in size from 3 to 56 nucleotides for RSV B strains (Fig. 3). The intergenic regions do not contain any conserved motifs or any obvious features of secondary structure and have been shown to have no influence on the preceding and succeeding gene expression in a minreplicon system (Fig. 3). The last two RSV genes overlap by 68 nucleotides (Fig. 3). The gene-start signal of the L gene is located inside of, rather than after, the M2 gene. This 68 nucleotide overlap sequence encodes the last 68 nucleotides of the M2 mRNA (exclusive of the Poly-A tail), as well as the first 68 nucleotides of the L mRNA.

Ten different species of subgenomic polyadenylated mRNAs and a number of polycistronic polyadenylated read-through transcripts are the products of genomic transcription (74). Transcriptional mapping studies using UV light mediated

genomic inactivation showed that RSV genes are transcribed in their 3' to 5' order from a single promoter near the 3' end (80). Thus, RSV synthesis appears to follow the single entry, sequential transcription model proposed for all Mononegavirales (16,81). According to this model, the polymerase (L) contacts genomic RNA in the nucleocapsid form at the 3' genomic promoter region and begins transcription at the first nucleotide. RSV mRNAs are co-linear copies of the genes, with no evidence of mRNA editing or splicing.

Sequence analysis of intracellular RSV mRNAs showed that synthesis of each transcript begins at the first nucleotide of the gene start signal (74). The 5' end of the mRNAs are capped with the structure m7G(5')ppp(5')<u>G</u>p (where the underlined G is the first template nucleotide of the mRNA) and the mRNAs are polyadenylated at their 3' ends (82). Both of these modifications are thought to be made co-transcriptionally by the viral polymerase. Three regions of the RSV 3' genomic promoter have been found to be important as cis acting elements (83). These regions are the first ten nucleotides (presumably acting as a promoter), nucleotides 21-25, and the gene start signal located at nucleotides 45-53 (83). Unlike other Paramyxovirinae, such as measles, Sendai and PIV-3, the remainder of the leader and non-coding region of NS1 gene of RSV was found to be highly tolerant of insertions, deletions and substitutions (83).

Additionally, by saturation mutagenesis (wherein each base is replaced independently by each of the other three bases and compared for translation and replication efficiencies) within the first 12 nucleotides of the 3' genomic promoter region, a U-tract located at nucleotides 6-10 was shown to be

highly inhibitory to substitutions (83). In contrast, the first five nucleotides were relatively tolerant of a number of substitutions and two of them at position four were up-regulatory mutations, resulting in a four- to 20-fold increase in RSV-CAT RNA replication and transcription. Using a bi-cistronic minireplicon system, gene-start and gene-end motifs were shown to be signals for mRNA synthesis and appear to be self contained and largely independent of the nature of adjoining sequence (84).

The L gene start signal lies 68 nucleotides upstream of the M2 gene-end signal, resulting in gene overlap (Fig. 3) (74). The presence of the M2 gene-end signal within the L gene results in a high frequency of premature termination of L gene transcripts. Full length L mRNA is much less abundant and is made when the polymerase fails to recognize the M2 gene-end motif. This results in much lower transcription of L mRNA. The gene overlap seems incompatible with a model of linear sequential transcription. It is not known whether the polymerase that exits the M2 gene jumps backward to the L gene-start signal or whether there is a second, internal promoter for L gene transcription (74). It is also possible that the L gene is accessible by a small fraction of polymerases that fail to start transcription at the M2 gene-start signal and slide down the M2 gene to the L gene-start signal.

The relative abundance of each RSV mRNA decreases with the distance of its gene from the promoter, presumably due to polymerase fall-off during sequential transcription (80). Gene overlap is a second mechanism that reduces the synthesis of full length L mRNA. Also, certain mRNAs have features that might reduce the efficiency of translation. The initiation codon for SH mRNA is in a suboptimal Kozak

sequence context, while the G ORF begins at the second methionyl codon in the mRNA.

RSV RNA replication is thought (74) to follow the model proposed from studies with vesicular stomatitis virus and Sendai virus (16,81). This involves a switch from the stop-start mode of mRNA synthesis to an antiterminator read-through mode. This results in synthesis of positive sense replication-intermediate (RI) RNA that is an exact complementary copy of genomic RNA. This serves in turn as the template for the synthesis of progeny genomes. The mechanism involved in the switch to the antiterminator mode is proposed to involve cotranscriptional encapsidation of the nascent RNA by N protein (16,81). RNA replication in RSV like other nonsegmented negative-strand RNA viruses is dependent on ongoing protein synthesis (85). Predicted RI RNA has been detected for the standard virus as well as RSV-CAT minigenome (74,85). RI RNA was 10-20 fold less abundant intracellularly than was the progeny genome both for the standard and the minigenome system. The nucleotide sequences (in positive strand, antigenomic, message sense) of various wild-type, vaccine and revertant RSV strains, as well as the deduced amino acid sequences of the RNA polymerase (L protein) of these RSV viruses, are set forth as follows with reference to the appropriate SEQ ID NOS. contained herein:

Virus	Nucleotide Sequence	L Protein Sequence
Wild-Type		
2B	SEQ ID NO:23	SEQ ID NO:24
18537	SEQ ID NO:25	SEQ ID NO:26
Vaccine		
2B33F	SEQ ID NO:27	SEQ ID NO:28
2B20L	SEQ ID NO:29	SEQ ID NO:30
Revertant		
2B33F TS(+)	SEQ ID NO:31	SEQ ID NO:32
2B20L TS(+)	SEQ ID NO:33	SEQ ID NO:34

Each RSV virus genome encodes an L protein that is 2,166 amino acids long. Genome length and other nucleotide information is as follows:

Virus	Genome		
Wild-Type	Length	L Start Codon	L Stop Codon
2B	15218	8502-8504	15000-15002
18537	15229	8509-8511	15007-15009
Vaccine			
2B33F	15219	8503-8505	15001-15003
2B20L	15219	8503-8505	15001-15003
Revertant			
2B33F TS(+)	15219	8503-8505	15001-15003
2B20L TS(+)	15219	8503-8505	15001-15003

As detailed in Example 3 (especially Tables 7 and 8) below, the key attenuating mutations for the RSV subgroup B 3' genomic promoter region are nucleotide 4 (C $\rightarrow$ G), and the insertion of an additional A in the stretch of A's at nucleotides 6-11 (in antigenomic

message sense). As also detailed in Example 3 below, the key potentially attenuating sites for the L protein of RSV are as follows: amino acid residues 353 (arginine → lysine), 451 (lysine → arginine), 1229 (aspartic acid → asparagine), 2029 (threonine → isoleucine) and 2050 (asparagine → aspartic acid). It is understood that the nucleotide changes responsible for these amino acid changes are not limited to those set forth in Example 3 below; all changes in nucleotides which result in codons which are translated into these amino acids are within the scope of this invention.

The attenuated viruses of this invention exhibit a substantial reduction of virulence compared to wild-type viruses which infect human and animal hosts. The extent of attenuation is such that symptoms of infection will not arise in most immunized individuals, but the virus will retain sufficient replication competence to be infectious in and elicit the desired immune response profile in the vaccinee.

The attenuated viruses of this invention may be used to formulate a vaccine. To do so, the attenuated virus is adjusted to an appropriate concentration and formulated with any suitable vaccine adjuvant, diluent or carrier. Physiologically acceptable media may be used as carriers. These include, but are not limited to: an appropriate isotonic medium, phosphate buffered saline and the like. Suitable adjuvants include, but are not limited to MPL™ (3-O-deacylated monophosphoryl lipid A; RIBI ImmunoChem Research, Inc., Hamilton, MT) and IL-12 (Genetics Institute, Cambridge, MA).

In one embodiment of this invention, the formulation including the attenuated virus is intended for use as a vaccine. The attenuated virus may be mixed

with cryoprotective additives or stabilizers such as proteins (e.g., albumin, gelatin), sugars (e.g., sucrose, lactose, sorbitol), amino acids (e.g., sodium glutamate), saline, or other protective agents. This mixture is maintained in a liquid state, or is then dessicated or lyophilized for transport and storage and mixed with water immediately prior to administration.

Formulations comprising the attenuated viruses of this invention are useful to immunize a human or animal subject to induce protection against infection by the wild-type counterpart of the attenuated virus. Thus, this invention further provides a method of immunizing a subject to induce protection against infection by an RNA virus of the Order Mononegavirales by administering to the subject an effective immunizing amount of a vaccine formulation incorporating an attenuated version of that virus as described hereinabove.

A sufficient amount of the vaccine in an appropriate number of doses must be administered to the subject to elicit an immune response. Persons skilled in the art will readily be able to determine such amounts and dosages. Administration may be by any conventional effective form, such as intranasally, parenterally, orally, or topically applied to any mucosal surface such as intranasal, oral, eye, vaginal or rectal surface, such as by an aerosol spray. The preferred means of administration is by intranasal administration.

In another embodiment of this invention, an isolated nucleic acid molecule having the complete viral nucleotide sequence of either the wild-type viruses or vaccine viruses described herein is used to generate oligonucleotide probes (from either positive strand antigenomic message sense or negative strand

complementary genomic sense) and to express peptides (from positive strand antigenomic message sense only), which are used to detect the presence of those wild-type virus and/or vaccine strains in samples of body fluids and tissues. The nucleotide sequences are used to design highly specific and sensitive diagnostic tests to detect the presence of the virus in a sample.

Polymerase chain reaction (PCR) primers are synthesized with sequences based on the viral wild-type or vaccine sequences described herein. The test sample is subjected to reverse transcription of RNA, followed by PCR amplification of selected cDNA regions corresponding to the nucleotide sequence described herein which have nucleotides which are distinct for a defined strain of virus. Amplified PCR products are identified on gels and their specificity confirmed by hybridization with specific nucleotide probes.

ELISA tests are used to detect the presence of antigens of the wild-type or vaccine viral strains. Peptides are designed and selected to contain one or more distinct residues based on the wild-type or vaccine sequences described herein. These peptides are then coupled to a hapten (e.g., keyhole limpet hemocyanin (KLH) and used to immunize animals (e.g., rabbits) for the production of monospecific polyclonal antibody. A selection of these polyclonal antibodies, or a combination of polyclonal and monoclonal antibodies can then be used in a "capture ELISA" to detect antigens produced by those viruses.

Samples of the Moraten measles virus vaccine strain were deposited by Applicants with the American Type Culture Collection, 12301 Parklawn Drive, Rockville, Maryland 20852, U.S.A., under the provisions of the Budapest Treaty for the Deposit of Microorganisms for the Purposes of Patent Procedures

("Budapest Treaty") and have been assigned ATCC accession number VR2587. Samples of the HPIV-3 virus Vero-grown cp45 vaccine strain were deposited by Applicants with the American Type Culture Collection, 12301 Parklawn Drive, Rockville, Maryland 20852, U.S.A., under the provisions of the Budapest Treaty and have been assigned ATCC accession number VR2588. Samples of the 2B wild-type RSV virus were deposited by Applicants with the American Type Culture Collection, 12301 Parklawn Drive, Rockville, Maryland 20852, U.S.A., under the provisions of the Budapest Treaty and have been assigned ATCC accession number VR2586.

Given these three deposited strains and the sequence information for these and other strains provided herein, one can use site-directed mutagenesis and rescue techniques described above to introduce mutations (or restore a wild-type genotype) of all the strains described herein, as well as taking these strains and making additional mutations from the panel of mutations set forth in Tables 3, 4 and 6-8 below.

In order that this invention may be better understood, the following examples are set forth. The examples are for the purpose of illustration only and are not to be construed as limiting the scope of the invention.

Examples

Standard molecular biology techniques are utilized according to the protocols described in Sambrook et al. (86).

Example 1
Measles

Moraten MV vaccine virus was grown once, directly from the Attenuvax™ vaccine vial (Lot #0716B), the Schwarz vaccine virus was grown once (Lot 96G04/M179 G41D), while the Zagreb and Rubeovax™ vaccine viruses were each grown twice in the Vero cells before RNAs were made for sequence analysis. MV wildtype isolate Montefiore (56) was passed 5-6 times in Vero cells before extraction of RNA materials and similarly, MV wildtype isolates 1977, 1983 (14) were grown 5-7 times before extracting materials for analysis. Edmonston wild-type isolate received from Dr. J. Beeler (CBER) (see Fig. 1) was the original Edmonston isolate already passaged seven times in human kidney cells and three times in Vero cells before receipt and further passaged once in Vero cells before using for sequence analysis.

RNA was prepared by infecting Vero cells at a multiplicity of infection (m.o.i.) of 0.1 to 1.0 and allowed to reach maximum cytopathology before being harvested. Total RNA from measles virus-infected cells was extracted using Trizol™ reagent (Gibco-BRL).

The total RNA isolated from Vero cell passage material was amplified by the Reverse Transcriptase-PCR (Perkin-Elmer/Cetus) procedure using measles (Edmonston B strain (19)) specific primer pairs spanning the 3' and 5' promoter regions and the L gene of the viral genome. Table 2 presents these primer sequences. The primers of SEQ ID NOS:35-54, 74, 77 and 78 are in antigenomic message sense. The primers of SEQ ID NOS:55-73, 75, 76 and 79 are in genomic negative-sense.

Table 2

Primers for PCR and Sequencing MV L Genes and Genomic Termini

$_{9047}$CATATCACTCACTCTGGGATGGAG$_{9070}$	(SEQ ID NO:35)
$_{9371}$TCAGAACATCAAGCACCGCC$_{9390}$	(SEQ ID NO:36)
$_{9741}$ACAGTCAAGACTGAGATGAG$_{9760}$	(SEQ ID NO:37)
$_{10001}$AAGAGTCAGATACATGTGGA$_{10020}$	(SEQ ID NO:38)
$_{10351}$ACATGAATCAGCCTAAAGTC$_{10370}$	(SEQ ID NO:39)
$_{10674}$CCGAAAGAGTTCCTGCGTTACGACC$_{10698}$	(SEQ ID NO:40)
$_{11083}$CAGTCCACACAAGTACCAGG$_{11102}$	(SEQ ID NO:41)
$_{11461}$GTCAGAAGCTGTGGACCATC$_{11480}$	(SEQ ID NO:42)
$_{11841}$AATATTGCTACAACAATGGC$_{11860}$	(SEQ ID NO:43)
$_{12196}$ACTCTTCATTCCTAGACTGG$_{12215}$	(SEQ ID NO:44)
$_{12542}$GTCCAATTATGACTATGAAC$_{12561}$	(SEQ ID NO:45)
$_{12891}$AGAACAGACATGAAGCTTGC$_{12910}$	(SEQ ID NO:46)
$_{13232}$CCAACAAGGAATGCTTCTAG$_{13251}$	(SEQ ID NO:47)
$_{13551}$ACAGCACTATCTATGATTGACCTGG$_{13575}$	(SEQ ID NO:48)
$_{13930}$GCAACATGGTTTACACATGC$_{13949}$	(SEQ ID NO:49)
$_{14280}$AGATTGAGAGTTGATCCAGG$_{14299}$	(SEQ ID NO:50)
$_{14629}$AGGAGATACTTAAACTAAGC$_{14648}$	(SEQ ID NO:51)
$_{14981}$TAAGCTTATGCCTTTCAGCG$_{15000}$	(SEQ ID NO:52)
$_{15337}$TTAACGGACCTAAGCTGTGC$_{15356}$	(SEQ ID NO:53)
$_{15671}$GAAACAGATTATTATGACGG$_{15690}$	(SEQ ID NO:54)
$_{9290}$CGGGCTATCTAGGTGAACTTCAGG$_{9267}$	(SEQ ID NO:55)
$_{9500}$ATTTGGATATGGAATATGAG$_{9481}$	(SEQ ID NO:56)
$_{9840}$ACTCAACTGAACTACCAGTG$_{9821}$	(SEQ ID NO:57)
$_{10181}$AAGAACATCATGTATTTCAG$_{10162}$	(SEQ ID NO:58)
$_{10549}$TTATCAACGCACTGCTCATG$_{10530}$	(SEQ ID NO:59)
$_{10919}$ATTTTCAGCAATCACTTGGCATGCC$_{10895}$	(SEQ ID NO:60)
$_{11280}$GCCTCTGTGCAAACAAGCTG$_{11261}$	(SEQ ID NO:61)
$_{11638}$TCTCTAGTTACTCTAGCAGC$_{11619}$	(SEQ ID NO:62)
$_{12010}$AGGTCGTTGTTTGTGAGGAG$_{11991}$	(SEQ ID NO:63)
$_{12361}$TCGTCCTCTTCTTTACTGTC$_{12342}$	(SEQ ID NO:64)

$_{12689}$CCGTCCTCGAGCTAGCCTCG$_{12670}$ (SEQ ID NO:65)
$_{13052}$CTCCTCCAGGCTCACATTGG$_{13033}$ (SEQ ID NO:66)
$_{13420}$GGGTTGGTACATAGCTCTGC$_{13401}$ (SEQ ID NO:67)
$_{13767}$CACCCATCTGATATTTCCCTGATGG$_{13743}$ (SEQ ID NO:68)
$_{14099}$TGGTTGACAGTACAAATCTG$_{14080}$ (SEQ ID NO:69)
$_{14460}$CTGAAATGGGAAGATTGTGC$_{14441}$ (SEQ ID NO:70)
$_{14820}$AGCAATCTACACTGCCTACC$_{14801}$ (SEQ ID NO:71)
$_{15180}$TCACAGATGATTCAATTATC$_{15161}$ (SEQ ID NO:72)
$_{15530}$GATCCTAGATATAAGTTCTC$_{15511}$ (SEQ ID NO:73)

$_{1}$ACCAAACAAAGTTGGGTAAGG$_{21}$ (SEQ ID NO:74)
GGGGGATCC$_{100}$ATCCCTAATCCTGCTCTTGTCCC$_{78}$ (SEQ ID NO:75)
$_{200}$GATTCCTCTGATGGCTCCAC$_{181}$ (SEQ ID NO:76)
$_{15721}$TAACAGTCAAGGAGACCAAAG$_{15741}$ (SEQ ID NO:77)
GGGAAGCTT$_{15801}$AACCCTAATCCTGCCCTAGGTGG$_{15823}$ (SEQ ID NO:78)
$_{15894}$ACCAGACAAAGCTGGGAATAGA$_{15873}$ (SEQ ID NO:79)

Overlapping PCR fragments of the complete viral genome were directly sequenced without cloning to achieve the consensus sequence, by the dideoxy terminator cycle sequencing method using both strands (ABI PRISM 377 sequencer and ABI PRISM sequencing Kit). To determine the sequence at the absolute termini, a ligation procedure described previously was used (55).

To test this hypothesis, the nucleotide sequences were determined for the non-protein coding regulatory regions and the L gene of the progenitor Edmonston wild-type MV isolate, for the available vaccine strains derived from this isolate, as well as for other wild-type strains. Nucleotide (in antigenomic, message sense) and amino acid differences were then compared and aligned as set forth in Tables 3-5 (differences are in italics):

Table 3

Differences in MV 3' Genomic Promoter Region Nucleotide Sequence

	Nucleotide number:			
Virus	26	42	50	96
Edmonston w-t	A	A	G	G
Vaccines:				
Rubeovax™	*T*	*C*	G	G
Moraten	*T*	*C*	G	G
Schwarz	*T*	*C*	G	G
Zagreb	*T*	*T*	G	*A*
AIK-C	*T*	*C*	G	G
Wild-Types:				
1977	A	A	*A*	G
1983	A	A	*A*	G
Montefiore	A	A	*A*	G

Table 4

Differences in MV L Nucleotides and Amino Acids Between Edmonston Wild-Type and Vaccine Strains

	331	1409	1624	1649	1717	1887	1936	2074	2114
Edmonston w-t	ATT	GCA	ACC	AGG	GAT	AAC	CAT	CAA	AGA
Mutation	ACT	ACA	*GCC*	ATG	GCT	*GAC*	TAT	CGA	AAA
Edmonston w-t	I	A	T	R	D	N	H	Q	R
Rubeovax™ vac.	I	A	T	*M*	*A*	*D*	H	Q	R
Moraten vac.	*T*	A	T	*M*	*A*	*D*	H	Q	*K*
Schwarz vac.	*T*	A	T	*M*	*A*	*D*	H	Q	*K*
Zagreb vac.	I	*T*	T	R	*A*	N	H	Q	R
AIK-C vac.	I	*T*	*A*	R	*A*	N	*Y*	*R*	R

Table 5

Differences in MV L Nucleotides and Amino Acids

Between Wild-Type Strains

	81	122	149	252	331	441	447	500	513	570	613
Edmonston w-t	GCC	GAT	GTT	ACA	ATT	AAA	AAA	GAT	GTG	AAA	TAC
Mutation	ACC	AAT	ATT	GCA	GTT	AGA	AGA	AAT	ATG	AAT	CAC
Edmonston w-t	A	D	V	T	I	K	K	D	V	K	Y
1977 w-t	A	*N*	V	T	*V*	K	K	D	*M*	K	Y
1983 w-t	*T*	D	*I*	T	I	K	K	*N*	*M*	*N*	*H*
Montefiore w-t	A	D	*I*	*A*	I	*R*	*R*	D	*M*	K	Y

	618	621	623	626	628	632	636	637	641	645	650
Edmonston w-t	GTC	AGT	AGG	AGA	GCA	ATA	CAA	GTA	GAC	GAT	ATG
Mutation	GCC	AAT	AAG	AAA	GAA	GTA	CAT	ATA	AAT	AAT	ATA
Edmonston w-t	V	S	R	R	A	I	Q	V	D	D	M
1977 w-t	A	*N*	R	R	A	I	Q	*I*	D	*N*	M
1983 w-t	V	S	*K*	R	A	I	*H*	V	D	D	M
Montefiore w-t	V	S	R	*K*	*E*	*V*	*H*	V	*N*	D	*I*

Table 5 (continued)

Differences in MV L Nucleotides and Amino Acids

Between Wild-Type Strains

	652	720	723	794	914	970	1044	1294	1569	1705	1745
Edmonston w-t	GCT	ATC	TAT	CGG	CGG	GCC	GGA	AGC	GTT	ATC	AAT
Mutation	*ACC*	*GTC*	*TGC*	*TGG*	CAG	*TCA*	AGA	ACC	ATT	*GTC*	AGT
Edmonston w-t	A	I	Y	R	R	A	G	S	V	I	N
1977 w-t	A	I	*C*	*W*	*Q*	A	G	S	V	I	N
1983 w-t	A	*V*	*C*	R	R	*S*	G	*T*	*I*	I	N
Montefiore w-t	*T*	*V*	*C*	R	R	A	*R*	S	V	*V*	*S*

	1860	1865	1936	2007	2013	2017	2030	2096	2119	2165
Edmonston w-t	GTA	TTC	CAT	GAC	GAT	ACT	AAT	ATA	AAG	GTC
Mutation	ATA	TAC	*TAT*	GGC	GGT	ATT	AGT	*GTA*	*CGG*	ATC
Edmonston w-t	V	F	H	D	D	T	N	I	K	V
1977 w-t	V	*Y*	H	D	D	T	N	I	K	V
1983 w-t	V	F	*Y*	D	*G*	*I*	N	I	*R*	*I*
Montefiore w-t	*I*	F	H	*G*	D	*I*	*S*	*V*	*R*	V

Example 2

PIV-3

A comparison of sequences (in antigenomic message sense) of the parental wild-type JS strain of PIV-3 virus and the FRhL-grown and Vero-grown forms of the cp45 mutant are set forth in Table 6. Where a codon change does not result in an amino acid change, Table 6 states "none", followed by the name of the unchanged amino acid.

Table 6
Sequence Comparison of Vero- and FRhL-grown cp45 & JS strains

Gene Region	Nucleotide Position	JS	FRhL cp45	Vero cp45	Codon Change	Amino Acid Change (number in L)
3' leader	23	T	C	C		
	24	C	T	T		
	28	G	T	T		
	45	T	A	A		
NP UTR	62	A	T	T		
NP coding	397	T	C	C	GTC → GCC	Val → Ala
	1275	T	G	G	TCT → GCT	Ser → Ala
P coding	2080	T	C	C	AAT → AAC	none/Asn
M coding	4347	C	A	A	CCC → ACC	Pro → Thr
F coding	5536	C	T	T	AAC → AAT	none/Asn
	6329	A	G	G	ATA → GTA	Ile → Val
	6419	G	A	A	GCA → ACA	Ala → Thr
HN coding	6847	T	C	C	GGT → GGC	none/Gly
	7956	T	C	C	GTT → GCT	Val → Ala
L coding	9323	T	C	C	TAT → TAC	none/Tyr (226)
	9971	A	G	G	GAA → GAG	none/Glu (442)
	11469	T	C	C	TAC → CAC	Tyr → His (942)
	11621	G	T	T	TTG → TTT	Leu → Phe (992)
	12521	A	A	T*	TTA → TTT	Leu → Phe (1292)
	12581	C	T	T	TTC → TTT	none/Phe (1312)
	13318	C	T	T	ACT → ATT	Thr → Ile (1558)
# mutations			20	21		

Sequence analysis of the parental wild-type JS strain of PIV-3 virus and the FRhL-grown cp45 mutant showed that the latter contained 20 nucleotide changes. Four changes were in the noncoding 3'-leader region at nucleotide positions 23 (T $\rightarrow$ C), 24 (C $\rightarrow$ T), 28 (G $\rightarrow$ T) and 45 (T $\rightarrow$ A) (in antigenomic, message sense). When considered in the genomic, negative sense, the change at position 28 from the smaller pyrimidine ("C") to the larger purine ("A") may change the size of the region flanked by the conserved regions of the 3' genomic promoter region, resulting in an altered spatial presentation of the cis-acting signals to the polymerase.

Nine changes were coding changes in the NP, M, F, HN and L genes. The other seven changes were non-coding or silent changes in the NP, P, F, HN and L genes or the NP untranslated region (UTR). The cp45 mutant has been demonstrated to have poor transcription activity at non-permissive temperatures due to its *ts* phenotype (87). This *ts* phenotype has now been mapped to the viral L gene (88). Because the cp45 virus has been shown to function normally with regard to mutations in the HN and F glycoproteins (87), this supports the implication that mutations in the 3'-leader and L gene contributed to the attenuating phenotype of this virus.

Thus, the four 3' leader specific changes in FRhL-grown cp45 and the three coding changes in the L gene at amino acid positions 942 (Tyr $\rightarrow$ His), 992 (Leu $\rightarrow$ Phe) and 1558 (Thr $\rightarrow$ Ile) contributed significantly to the attenuation phenotype of the candidate cp45 vaccine strain.

Furthermore, the Vero-grown cp45 mutant vaccine strain contains an additional mutation resulting from a coding change in the L gene (marked

with an asterisk in Table 6) at amino acid residue 1292 (leucine → phenylalanine).

The first two amino acid changes in the L protein (at positions 942 and 992) map to one of the highly conserved areas among all Paramyxovirus L genes. The fourth amino acid change (at position 1558) maps to the area joining two conserved blocks corresponding to the change at amino acid 1717 in the MV vaccine strains.

The published literature (89) sets forth only 18 changes between the antigenomic message sense sequences of the JS and FRhL-grown cp45 strains. Sixteen of these changes were found by applicants.

The published literature did not report four changes found by applicants: in the 3′ leader at nucleotide 45 (T → A), in the NP UTR at nucleotide 62 (A → T), or the changes in amino acids in the NP protein resulting from the changes at nucleotide 397 (T → C), leading to the amino acid change (Val → Ala) and nucleotide 1275 (T → G), leading to the amino acid change (Ser → Ala) (nucleotide changes in antigenomic, message sense). Nor did the published literature report the additional potentially attenuating mutation in the L protein found by applicants in the Vero-grown cp45 strain resulting from the change at nucleotide 12521 (A → T), leading to the change in amino acid 1292 (Leu → Phe).

Example 3

RSV Subgroup B

The temperature-sensitive (*ts*) phenotype is strongly associated with attenuation *in vivo*; in addition, some non-*ts* mutations may also be attenuating. Identification of *ts* and non-*ts* attenuating mutations was achieved by sequence analysis and evaluation of *ts*, cold-adapted (*ca*), and *in vivo* growth phenotypes of RSV mutants and revertants.

The genomes of the following five RSV 2B strains have now been completely sequenced: 2B parent, 2B33F, one revertant designated 2B33F TS(+), 2B20L and one revertant designated 2B20L TS(+). The 2B33F and 2B20L strains are *ts* and *ca* and are described in U.S. Serial No. 08/059,444 (90), which is hereby incorporated by reference. After identifying regions where mutations in 2B33F and 2B20L are located, nine additional isolates of 2B33F "revertants" obtained following *in vitro* passaging at 39°C and *in vivo* passaging in African Green Monkeys or chimpanzees, and nine additional isolates of 2B20L "revertants" obtained following *in vitro* passaging at 39°C have been sequenced in those regions. The *ts*, *ca*, and attenuation phenotypes of many of these revertants have now been characterized and assessed. Correlations between phenotype *ts*, vaccine attenuation and sequence changes have been identified.

A summary of results is presented in Tables 7-12.

Table 7

Sequence comparison between RSV 2B and 2B33F strains

Gene/ region	Nucl. pos.† 3' end of vRNA	Nucleotide changes RSV 2B	RSV 2B33F	RSV 2B33F TS(+), 5a revertant	Amino acid changes
Genomic Promoter	4	C	G	G	non-coding
	6	-	extra A	extra A	non-coding
M	4175	T	C	C	non-coding
	4199	T	C	C	non-coding
SH	4329	T	C	C	Phe-Leu (10)
	4409	T	C	C	none Ile (36)
	4420	T	C	C	Ile-Thr (40)
	4442	T	C	C	none His (47)
	4454	T	C	C	none Cys (51)
	4484	T	C	C	none Tyr (61)
	4497	T	C	C	Stop-Gln (66)
	4505	T	C	C	none Ser (68)
	4525	T	C	C	Ile-Thr (75)
	4526	T	C	C	Ile-Thr (75)
	4542	T	C	C	Stop-Gln (81)
	4561	T	C	C	Leu-Pro (87)
	4575	T	C	C	Trp-Arg (92)
	4598	T	C	C	none Thr (99)
L	9559	G	A	A	Arg-Lys (353)
	9853*	A	G	A	Lys-Arg (451)*
	12186	G	A	A	Asp-Asn (1229)
	14587	C	T	T	Thr-Ile (2029)
	15071	A	G	G	non-coding

† For 2B33F and 2B33F TS(+), nucl. pos. numbers are one larger than for 2B for M, SH & L genes

* At pos. 9853, the Lys-Arg change has reverted back to Lys in the 2B33F TS(+) strain

Table 8

Sequence comparison between RSV 2B and 2B20L strains

	Nucl. pos.†	Nucleotide changes			
Gene/ region	3' end of vRNA	RSV 2B	RSV 2B20L	RSV 2B20L TS(+), R1 revertant	Amino acid changes
Genomic Promoter	4 6	C -	G extra A	G extra A	non-coding* non-coding*
L	8963 13347 14587 14649 14650	C A C A A	T A T G A	T G T G T	none Thr (154) Asn-Asp (1616) Thr-Ile(2029)* Asn-Asp (2050) Asn-Asp-Val (2050)**

† For 2B20L and 2B20L TS(+), nucl. pos. numbers are one larger than for 2B for L gene

* Mutation is common in 2B33F and 2B20L strains

** At pos. 14650, the mutation suppresses the ts phenotype in 2B20L TS(+) revertant

Table 9

RSV 2B, ts and Revertant Strains

Sample	Source	In Vitro Phenotype ts	In Vitro Phenotype ca	In Vivo Growth* Cotton Rat		AGM	
		39/32°C EOP plaque morph	20/32°C Yield	Nasal turbinates	Lungs	Nasal Wash	Bronchial Lavage
RSV 2B	Wild-type Parent Strain	0.7 (WT)	0.0001	5.5^{a} 3.9^{b} (4/4)	5.8^{a} 5.2^{b} (4/4)	5.8^{c} (4/4)	4.7^{c} (4/4)
RSV 2B33F	*ca, ts* mutant isolated from 2B cold-passaged x 33	0.00007 (sp/int/wt)	0.04	$\leq 1.6^{a}$ $<1.9^{b}$ (1/4)	$<1.5^{a}$ $<1.2^{b}$ (0/4)	3.0^{c} (4/4)	$<0.9^{c}$ (0/4)
RSV 2B33F - 5a TS(+)	2B33F spinner passage, plaque picked at 39°C	0.5 (WT)	0.03	$\leq 1.7^{a}$ (1/4)	3.5^{a} (4/4)	4.2^{c} (4/4)	4.0^{c} (4/4)
RSV 2B33F - 4a TS(+)	2B33F spinner passage, plaque picked at 39°C	0.7 (WT)	0.01	$\leq 1.7^{a}$ (3/4)	3.8^{a} (4/4)	ND	ND
RSV 2B33F - 3b TS(+)	2B33F spinner passage, plaque picked at 39°C	0.5 (WT)	0.04	$\leq 2.5^{a}$ (3/4)	2.9^{a} (4/4)	ND	ND
AGM pp2	2B33F-infected AGM #A2,d7 nasal wash plaque picked at 32°C	0.3 (sp,int)	0.00002	$\leq 2.0^{b}$ (1/4)	1.6^{b} (4/4)	ND	ND

Table 9 (continued)
RSV 2B, *ts* and Revertant Strains

Sample	Source	*In Vitro* Phenotype *ts*	*ca*	*In Vivo* Growth* Cotton Rat		AGM	
		39/32°C EOP plaque morph	20/32°C Yield	Nasal turbinates	Lungs	Nasal Wash	Bronchial Lavage
AGM pp4	2B33F-infected AGM #A2,d7 nasal wash plaque picked at 32°C	0.1 (sp,int)	0.008	<1.6[b] (0/4)	1.2[b] (4/4)	ND	ND
AGM pp6	2B33F-infected AGM #A4,d12 nasal wash plaque picked at 32°C	0.000004 (wt)	≤0.00005	≤1.5[b] (1/4)	<1.1[b] (0/4)	ND	ND
AGM pp7	2B33F-infected AGM #A4,d12 nasal wash plaque picked at 32°C	0.000004 (sp/int/wt)	0.007	≤1.4[b] (1/4)	<1.0[b] (0/4)	ND	ND
Chimp pp1A	2B33F-infected Chimp #1552, d4 tracheal lavage plaque picked at 32°C	0.5 (WT)	ND	ND	ND	ND	ND
Chimp pp3A	2B33F-infected Chimp #1560, d6 tracheal lavage plaque picked at 32°C	0.7 (WT)	ND	2.4[c] (4/4)	≤3.0[c] (3/4)	ND	ND
Chimp pp5A	2B33F-infected Chimp #1563, d10 nasal swab plaque picked at 32°C	0.7 (WT)	ND	≤2.3[c] (3/4)	3.0[c] (4/4)	ND	ND

Table 9 (continued)
RSV 2B, *ts* and Revertant Strains

Sample	Source	*In Vitro* Phenotype *ts*	*ca*	*In Vivo* Growth* Cotton Rat		AGM	
		39/32°C EOP plaque morph	20/32°C Yield	Nasal turbinates	Lungs	Nasal Wash	Bronchial Lavage
RSV 2B20L	*ca*, *ts* mutant isolated from 2B cold-passaged x 20	0.0002 (int/wt)	0.02	<1.9[d] (0/4)	<1.3[d] (0/4)	<0.7[f] (0/2)	<0.7[f] (0/2)
RSV 2B20L R1 TS(+)	2B20L spinner passage, plaque picked at 39°C	0.6 (WT)	ND	2.3[c] (4/4)	3.5[c] (4/4)	ND	ND
RSV 2B20L R2 TS(+)	2B20L spinner passage, plaque picked at 39°C	0.6 (WT)	ND	≤2.5[c] (3/4)	2.7[c] (4/4)	ND	ND
RSV 2B20L R9 TS(+)	2B20L spinner passage, plaque picked at 39°C	0.8 (WT)	ND	≤2.2[c] (3/4)	4.0[c] (4/4)	ND	ND
RSV 2B20L R10 TS(+)	2B20L spinner passage, plaque picked at 39°C	0.7 (WT)	ND	2.6[c] (4/4)	3.2[c] (4/4)	ND	ND

* In Vivo growth measured in log_{10} mean virus titer (# infected/# total)
ND = not done WT = wild-type plaque size sp = small plaque size int = intermediate plaque size
[a] Dose = $10^{6.7}$ PFU IN [b] Dose = $10^{5.6}$ PFU IN [c] Dose = $10^{6.3}$ PFU IN
[d] Dose = $10^{5.9}$ PFU IN [e] Dose = $10^{6.6}$ PFU IN+IT [f] Dose = $10^{6.0}$ PFU IN+IT

Table 10

2B33F Revertants

	ts (+) *In vitro*			AGM				Chimp		
	5a	4a	3b	pp2	pp4	pp6	pp7	1A	3A	5A
base no.†										
M										
4176,4200	S	S	S	S	S	S	S	S	S	S
SH										
14 bases*	S	S	S	S	S	S	S	S	S	S
L										
9560	S	S	S	S	S	S	S	S	S	S
9854	2B	2B	2B	2B	S	S	S	ND	2B	2B
12187	S	S	S	S	S	S	S	S	S	S
14588	S	S	S	S	S	S	S	ND	S	S
15072	S	S	S	S	S	S	S	S	S	S
Phenotype										
ts	2B	2B	2B	r	r	S	S	2B	2B	2B
ca	S	S	S	2B	S	2B	S	ND	ND	ND
Attenuated	r	r	r	(r)	(r)	S	S	ND	r	r

† These 2B33F revertant base nos. are one larger than for 2B for M, SH and L genes

* bases 4330,4410,4421,4443,4455,4485,4498,4506,4526,4527,4543, 4562,4576,4599

S = same base as 2B33F

2B = reversion to 2B base or complete reversion in phenotype

r = moderate reversion in phenotype

(r) = slight reversion in phenotype

ND = not done

Table 11

2B20L Revertants

	TS(+) *In vitro* Isolates									
base no.†	R1	R2	R3A	R4A	R5A	R6A	R7A	R8A	R9A	R10A
L										
8964	S	S	S	S	S	S	S	S	S	S
13348	C*	S	ND	S	S	ND	S	S	S	S
14588	S	S	S	S	S	S	S	S	S	S
14650	S	S	2B	S	2B	2B	S	S	2B	2B
14651	A*	A*	S	A*	S	S	A*	A*	S	S
Phenotype										
ts	2B	2B	ND	ND	ND	ND	ND	ND	2B	2B
Attenuated	r	r	ND	ND	ND	ND	ND	ND	r	r

† These 2B20L revertant base nos. are one larger than for 2B for L genes

S = same base as 2B20L

2B = reversion to 2B base

r = moderate reversion in phenotype

* = base change, different from 2B or 2B20L

ND = not done

Table 12
RSV 2B, *ts* and Revertant Strains: Phenotype Summary

Virus Isolate	Source	*In Vitro* Phenotype *ts*	*In Vitro* Phenotype *ca*	*In Vivo* Attenuation Cotton Rat	*In Vivo* Attenuation AGM
RSV 2B	Wild-type Parent Strain	-	-	-	-
RSV 2B33F	*ca, ts* mutant isolated from 2B, cold-passaged x 33	++++	++	++++	+++
RSV 2B33F - 5a TS(+)	2B33F spinner passage plaque picked at 39°C	-	++	++	+
RSV 2B33F - 4a TS(+)	2B33F spinner passage plaque picked at 39°C	-	++	++	ND
RSV 2B33F - 3b TS(+)	2B33F spinner passage plaque picked at 39°C	-	++	++	ND
AGM pp2	2B33F-infected AGM A2, d7 nasal wash plaque picked at 32°C	+	-	+++	ND
AGM pp4	2B33F-infected AGM A2, d7 nasal wash plaque picked at 32°C	+	++	+++	ND
AGM pp6	2B33F-infected AGM A4, d12 nasal wash plaque picked at 32°C	++++	-	++++	ND
AGM pp7	2B33F-infected AGM A4, d12 nasal wash plaque picked at 32°C	++++	++	++++	ND
Chimp pp1A	2B33F-infected chimp #1552, d4 tracheal lavage, plaque picked at 32°C	-	ND	ND	ND
Chimp pp3A	2B33F-infected chimp #1560, d6 tracheal lavage, plaque picked at 32°C	-	ND	++	ND
Chimp pp5A	2B33F-infected chimp #1563, d10 tracheal lavage, plaque picked at 32°C	-	ND	++	ND

Table 12 (continued)
RSV 2B, *ts* and Revertant Strains: Phenotype Summary

Virus Isolate	Source	*In Vitro* Phenotype *ts*	*ca*	*In Vivo* Attenuation Cotton Rat	AGM
RSV 2B20L	*ca, ts* mutant isolated from 2B, cold-passaged x 20	++++	++	++++	++++
RSV 2B20L R1 TS(+)	2B20L spinner passage plaque picked at 39°C	-	ND	++	ND
RSV 2B20L R2 TS(+)	2B20L spinner passage plaque picked at 39°C	-	ND	++	ND
RSV 2B20L R9 TS(+)	2B20L spinner passage plaque picked at 39°C	-	ND	++	ND
RSV 2B20L R10 TS(+)	2B20L spinner passage plaque picked at 39°C	-	ND	++	ND

ND = not done
- = wild-type phenotype, i.e., not temperature sensitive, not cold adapted, not attenuated
+ to ++++ = increasing levels of temperature sensitivity, cold-adaptation or attenuation

Several significant observations can be drawn from these data:

a. As shown in Tables 7 (for 2B33F) and 8 (for 2B20L), there are relatively few sequence changes identified in the two mutant strains: RSV 2B33F differs from parental RSV 2B by two changes at the 3' genomic promoter region, two changes at the non-coding 5'-end of the M gene, and four coding changes plus one non-coding (poly(A) motif) change in the RNA dependent RNA polymerase coding L gene. In addition, 14 changes mapped to the SH gene alone. RSV 2B20L differs from its RSV 2B parent only at seven nucleotide positions, of which three are common with 2B33F virus, including two changes at the 3' genomic promoter and one coding change in the L gene. Two additional unique changes of 2B20L virus mapped to the coding region of the L gene. Potentially attenuating mutations at the non-coding 3' genomic promoter region and the RNA dependent RNA polymerase gene have been identified.

b. Two *ts* mutations can be identified in the L gene of the attenuated virus strains 2B33F and 2B20L:

(i) In 2B33F, a mutation at nucleotide position 9853 (A $\rightarrow$ G) leading to a coding change in L protein at amino acid 451 (Lys $\rightarrow$ Arg) is clearly associated with the *ts* and attenuation phenotypes. Reversion at this site alone in the 2B33F TS(+) 5a strain is responsible for complete restoration of growth at 39°C (Table 9) and partial reversion in attenuation in animals. This association with the *ts* and attenuation phenotypes was also supported by partial sequence analyses of six additional "full TS revertants" (designated 4a, 3b, pp2, 3A, 5a, 5A) isolated from cell

culture and from chimps, in which only the nucleotide 9853 mutation reverted (Tables 10-12) (note that one AGM (African Green Monkey) isolate which reverted at 9853 only partially reverted in *ts* phenotype). This amino acid 451 mutation (Lys $\rightarrow$ Arg) is amenable to stabilization in cDNA infectious clone constructs, by inserting a second mutation to stabilize the codon, thereby lessening the likelihood that it will revert back to Lys.

(ii) In 2B20L, a mutation at base 14,649 (A $\rightarrow$ G) leading to a coding change in the L protein (amino acid position 2,050, Asn $\rightarrow$ Asp) appears to be associated with the *ts* and attenuation phenotypes. This aspartic acid at the amino acid 2050 invariably reverts back (Asp $\rightarrow$ Asn) in TS(+) revertants or changes to a different amino acid (Asp $\rightarrow$ Val) by nucleotide substitution at position 14,650 (A $\rightarrow$ T) (Tables 8, 11). The above observation is based on complete sequence analysis on the TS(+) revertant R1 and partial sequence of several additional TS(+) revertants (R2, R4A, R7A, R8A) at selected regions (Table 11). An additional mutation is seen in the R1 revertant at nucleotide postion 13,347 (amino acid 1616, Asn $\rightarrow$ Asp) associated with the above reversion. However, the effect of this mutation on the *ts* phenotype is not known; the L gene of other revertants has not been sequenced completely.

c. Three base changes are common to 2B33F and 2B20L strains of virus:

(i) A change at position 14,587 (C $\rightarrow$ T) with a corresponding change (Thr $\rightarrow$ Ile) at amino acid 2029 is

present in both 2B33F and 2B20L (Tables 7,8). This nucleotide "T" substitution was found to be present in 10% of the population of the progenitor RSV2B strain and may have been preferred during the attenuation process. No wildtype base "C" was found in the 2B33F and 2B20L virus.

(ii) Two mutations are seen in the 2B33F and 2B20L 3' genomic promoter region: nucleotide 4 (C $\rightarrow$ G) and the insertion of an extra A in the stretch of A's at positions 6-11 (in antigenomic, message sense). When the sequences of selected TS(+) revertants were analyzed, these mutations were seen to have been retained in the 2B33F TS(+)5a (Table 7) and the 2B20L TS(+)R1 (Table 8) revertants. These non-coding, cis-acting mutations remained associated with partial viral attenuation.

Expression using the minireplicon RSV-CAT system for the analysis of these cis-acting changes has shown the 3' genomic promoter nucleotide 4 (C $\rightarrow$ G) change to be an upregulation of transcription/replication in this *in vitro* system when the 2B progenitor virus or either of the 2B33F or 2B33F TS(+) provided helper L gene functions (the N, P and M2 genes are identical in these viruses).

Complementation analysis of the 2B33F 3' genomic promoter and the helper functions provided by the progenitor RSV2B virus or the 2B33F and 2B33F TS(+) viruses by this RSV-CAT minireplicon system has also been conducted. All three viruses supported both the 2B and 2B33F 3' genomic promoter mediated transcription/replication functions. However, the 2B33F and 2B33F TS(+) viruses preferred their 2B33F 3' genomic promoters. This analysis clearly shows co-evolution of 3' genomic promoter changes during the

vaccine attenuation process, along with the RNA dependent RNA polymerase gene. Reversion of *ts* phenotype in the 2B33F mutant 5a by reversion of the single L protein amino acid 451 (Arg $\rightarrow$ Lys) by sequence analysis was clearly demonstrated by support of transcription/replication functions of RSV-CAT minireplicon at 37°C. The 2B33F virus did not provide helper functions to the RSV-CAT minireplicon (with 2B or 2B33F 3' genomic promoters) at 37°C.

d. A biased hypermutation of SH seen in 2B33F is present in all 2B33F revertants, regardless of phenotype, and is not seen in 2B20L, which is *ts*, *ca*, and attenuated. Thus, there are no data at this time that associate this mutation with any biological phenotype.

Another wild-type RSV designated 18537 was also sequenced and compared to the sequence of the wild-type RSV 2B strain. With one exception, at all the critical residues described above, the two wild-type strains were identical. For 2B, the codon ACA at nucleotides 14586-14588 encodes a Thr at amino acid 2029 of the L protein, while for 18537, the codon ATT at nucleotides 14593-14595 encodes an Ile at amino acid 2029 (the L gene start codon is at nucleotides 8509-8511 in 18537, compared to 8502-8504 in 2B).

Example 4

PCR Assay to Detect Measles Virus

A 21 year old patient was admitted to a hospital with a three week history of progressive non-productive cough, shortness of breath, and fever. His symptoms failed to improve following treatment with clarithromycin for seven days or after a similar course

of treatment with atovaquone. Concomitant complaints of right upper quadrant abdominal pain proved recalcitrant to omeprazole and antacids. Relevant past medical history included Factor VIII deficiency and HIV infection diagnosed 3-4 years prior to this hospital admission. One year earlier, he had received a booster immunization of measles-mumps-rubella (MMR) vaccine as required for college enrollment.

Bronchoalveolar lavage and transbronchial biopsies performed two days after admission to the hospital demonstrated reactive hyperplasia and alveolar lining cell desquamation with minimal chronic inflammation. No microorganisms were revealed by Gram, methenamine silver, or PAS stains. CT scans of the chest showed multiple, ill-defined, confluent nodules at the left lung base. Despite administration of empiric antimicrobials for opportunistic bacterial, mycobacterial, and fungal pathogens commonly responsible for pulmonary complications of advanced HIV disease, the patient became and remained febrile to 39°C. A left-sided pleural effusion developed; diagnostic thoracentesis showed it to be exudative but otherwise non-diagnostic. Bronchoalveolar lavage performed three weeks later only demonstrated alveolar histiocytes, some of which were hemosiderin laden, a few lymphocytes, and neutrophils. FITE, AFB, and methanamine silver stains again were negative.

Two weeks thereafter, a wedge resection of the left lung was performed through CT-guided minithoracotomy. Multiple tissue sections revealed nodular areas of acute and chronic inflammation with regions of necrosis and fibrosis. Numerous multinuclated giant cells were present, some of which contained both intracytoplasmic and intranuclear inclusions suggestive of measles virus giant cell

pneumonia. Special stains for bacteria, fungi, *P. carinii*, and acid fast organisms again gave negative results. Electron microscopic examination of sections of this lung biopsy revealed particles morphologically consistent with paramyxoviruses such as measles virus. Serum anti-measles IgM titers determined by a solid phase hemadsorbant assay were negative, as was a subsequent IgM capture immunoassay.

Two weeks later, Rhesus monkey kidney (RMK) tissue culture cells inoculated with the patient's lung biopsy material revealed cytopathic changes characteristic of measles virus infection. Confirmation was obtained using an immunofluorescence assay with monoclonal antibodies directed to measles virus. Based upon this diagnosis, oral ribavirin 1000mg B.I.D. was given for 14 days. Unfortunately, the patient progressively deteriorated, eventually dying two months later.

In order to ascertain the nature of the measles virus present in the patient, reverse transcription and PCR amplification of virus obtained from infected tissues were performed, followed by sequence analysis. The measles virus isolated from Rhesus monkey kidney cells inoculated with tissue from this patient's lung biopsy was propagated by two serial passages in the continuous Vero (monkey kidney) tissue culture cell line. Total infected cell RNA was extracted at the second Vero cell passage using TRIzol reagent (Life Technologies, Grand Island, NY) according to the manufacturer's protocol. Total RNA was similarly extracted from the patient's lung biopsy material. The measles virus vaccine strain (Moraten) currently used in the United States as a component of the trivalent MMR vaccines, was obtained in its univalent form (Attenuvax™, Merck, Sharpe, & Dohme).

This virus was passaged once in Vero cells and total vaccine infected cellular RNA then was extracted as described above.

Each of these RNA preparations was reverse transcribed (RT) to cDNA using random hexameric primers and Maloney murine leukemia virus reverse transcriptase (Perkin-Elmer/Cetus RT-PCR kit reagents, Perkin-Elmer-Cetus, Branchburg, NJ). The cDNA then was amplified by PCR using measles virus-specific oligodeoxynucleotide primer pairs whose design was based on the Edmonston measles virus sequence described above. These PCR products comprised a set of overlapping DNA fragments spanning the entire 15,894 nucleotide long measles genome. A consensus genomic sequence was established by direct analysis of each PCR product, without cloning, using the dideoxy terminator cycle-sequencing method established by the manufacturer (ABI PRISM 377 sequencer and ABI PRISM DNA sequencing kit; Perkin-Elmer/Cetus, Foster City, CA). Both strands of the PCR-amplified DNA products were analyzed to eliminate possible sequencing ambiguities.

The nucleotide sequences of selected regions of the measles virus genomes present in the patient's viral isolate, as well as in the diseased lung tissue, were compared with that of the Moraten vaccine virus, as well as with the nucleotide sequences of other measles virus wild-type and vaccine strains. This sequence analysis revealed identity to the Moraten vaccine strain rather than demonstrating relatedness to past or currently circulating wild-type viruses or other measles vaccine strains.

Example 5
ELISA to Detect RSV

An ELISA test is used to detect the presence of RSV. Peptides are designed and selected based on homologies to the RSV sequences described herein to be specific for all subgroup B strains, or for individual wild-type, vaccine or revertant RSV subgroup B strains described herein. These peptides are then coupled to KLH and used to immunize rabbits for the production of monospecific polyclonal antibody. A selection of these polyclonal antibodies, or a combination of polyclonal and monoclonal antibodies is then used in a "capture ELISA" to detect the presence of an RSV antigen.

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90. U.S. Patent Application No. 08/059,444.

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(2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 15894 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

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AACTGATAGA TGGTTTCTTC CCTGCACTCG GGAATCCAAC TTATCAAATT GTAGCCATGC 10080

TGGAGCCTCT TTCACTTGCT TACCTGCAGC TGAGGGATAT AACAGTAGAA CTCAGAGGTG 10140

CTTTCCTTAA CCACTGCTTT ACTGAAATAC ATGATGTTCT TGACCAAAAC GGGTTTTCTG 10200

ATGAAGGTAC TTATCATGAG TTAATTGAAG CTCTAGATTA CATTTTCATA ACTGATGACA 10260

TACATCTGAC AGGGGAGATT TTCTCATTTT TCAGAAGTTT CGGCCACCCC AGACTTGAAG 10320

CAGTAACGGC TGCTGAAAAT GTTAGGAAAT ACATGAATCA GCCTAAAGTC ATTGTGTATG 10380

AGACTCTGAT GAAAGGTCAT GCCATATTTT GTGGAATCAT AATCAACGGC TATCGTGACA 10440

GGCACGGAGG CAGTTGGCCA CCGCTGACCC TCCCCCTGCA TGCTGCAGAC ACAATCCGGA 10500

ATGCTCAAGC TTCAGGTGAA GGGTTAACAC ATGAGCAGTG CGTTGATAAC TGGAAATCTT 10560

TTGCTGGAGT GAAATTTGGC TGCTTTATGC CTCTTAGCCT GGATAGTGAT CTGACAATGT 10620

ACCTAAAGGA CAAGGCACTT GCTGCTCTCC AAAGGGAATG GGATTCAGTT TACCCGAAAG 10680

AGTTCCTGCG TTACGACCCT CCCAAGGGAA CCGGGTCACG GAGGCTTGTA GATGTTTTCC 10740

TTAATGATTC GAGCTTTGAC CCATATGATG TGATAATGTA TGTTGTAAGT GGAGCTTACC 10800

TCCATGACCC TGAGTTCAAC CTGTCTTACA GCCTGAAAGA AAAGGAGATC AAGGAAACAG 10860

GTAGACTTTT TGCTAAAATG ACTTACAAAA TGAGGGCATG CCAAGTGATT GCTGAAAATC 10920

TAATCTCAAA CGGGATTGGC AAATATTTTA AGGACAATGG GATGGCCAAG GATGAGCACG 10980

ATTTGACTAA GGCACTCCAC ACTCTAGCTG TCTCAGGAGT CCCCAAAGAT CTCAAAGAAA 11040

GTCACAGGGG GGGGCCAGTC TTAAAAACCT ACTCCCGAAG CCCAGTCCAC ACAAGTACCA 11100

GGAACGTGAG AGCAGCAAAA GGGTTTATAG GGTTCCCTCA AGTAATTCGG CAGGACCAAG 11160

ACACTGATCA TCCGGAGAAT ATGGAAGCTT ACGAGACAGT CAGTGCATTT ATCACGACTG 11220

ATCTCAAGAA GTACTGCCTT AATTGGAGAT ATGAGACCAT CAGCTTGTTT GCACAGAGGC 11280

TAAATGAGAT TTACGGATTG CCCTCATTTT TCCAGTGGCT GCATAAGAGG CTTGAGACCT 11340

CTGTCCTGTA TGTAAGTGAC CCTCATTGCC CCCCCGACCT TGACGCCCAT ATCCCGTTAT 11400

ATAAAGTCCC CAATGATCAA ATCTTCATTA AGTACCCTAT GGGAGGTATA GAAGGGTATT 11460

GTCAGAAGCT GTGGACCATC AGCACCATTC CCTATCTATA CCTGGCTGCT TATGAGAGCG 11520

GAGTAAGGAT TGCTTCGTTA GTGCAAGGGG ACAATCAGAC CATAGCCGTA ACAAAAAGGG 11580

TACCCAGCAC ATGGCCCTAC AACCTTAAGA AACGGGAAGC TGCTAGAGTA ACTAGAGATT 11640

ACTTTGTAAT TCTTAGGCAA AGGCTACATG ATATTGGCCA TCACCTCAAG GCAAATGAGA 11700

CAATTGTTTC ATCACATTTT TTTGTCTATT CAAAAGGAAT ATATTATGAT GGGCTACTTG 11760

TGTCCCAATC ACTCAAGAGC ATCGCAAGAT GTGTATTCTG GTCAGAGACT ATAGTTGATG 11820

AAACAAGGGC AGCATGCAGT AATATTGCTA CAACAATGGC TAAAAGCATC GAGAGAGGTT 11880

ATGACCGTTA CCTTGCATAT TCCCTGAACG TCCTAAAAGT GATACAGCAA ATTCTGATCT 11940

CTCTTGGCTT CACAATCAAT TCAACCATGA CCCGGGATGT AGTCATACCC CTCCTCACAA 12000

ACAACGACCT CTTAATAAGG ATGGCACTGT TGCCCGCTCC TATTGGGGGG ATGAATTATC 12060

TGAATATGAG CAGGCTGTTT GTCAGAAACA TCGGTGATCC AGTAACATCA TCAATTGCTG 12120

ATCTCAAGAG AATGATTCTC GCCTCACTAA TGCCTGAAGA GACCCTCCAT CAAGTAATGA 12180

CACAACAACC GGGGGACTCT TCATTCCTAG ACTGGGCTAG CGACCCTTAC TCAGCAAATC 12240

TTGTATGTGT CCAGAGCATC ACTAGACTCC TCAAGAACAT AACTGCAAGG TTTGTCCTGA 12300
TCCATAGTCC AAACCCAATG TTAAAAGGAT TATTCCATGA TGACAGTAAA GAAGAGGACG 12360
AGGGACTGGC GGCATTCCTC ATGGACAGGC ATATTATAGT ACCTAGGGCA GCTCATGAAA 12420
TCCTGGATCA TAGTGTCACA GGGGCAAGAG AGTCTATTGC AGGCATGCTG GATACCACAA 12480
AAGGCCTGAT TCGAGCCAGC ATGAGGAAGG GGGGGTTAAC CTCTCGAGTG ATAACCAGAT 12540
TGTCCAATTA TGACTATGAA CAATTCAGAG CAGGGATGGT GCTATTGACA GGAAGAAAGA 12600
GAAATGTCCT CATTGACAAA GAGTCATGTT CAGTGCAGCT GGCGAGAGCT CTAAGAAGCC 12660
ATATGTGGGC GAGGCTAGCT CGAGGACGGC CTATTTACGG CCTTGAGGTC CCTGATGTAC 12720
TAGAATCTAT GCGAGGCCAC CTTATTCGGC GTCATGAGAC ATGTGTCATC TGCGAGTGTG 12780
GATCAGTCAA CTACGGATGG TTTTTTGTCC CCTCGGGTTG CCAACTGGAT GATATTGACA 12840
AGGAAACATC ATCCTTGAGA GTCCCATATA TTGGTTCTAC CACTGATGAG AGAACAGACA 12900
TGAAGCTTGC CTTCGTAAGA GCCCCAAGTC GATCCTTGCG ATCTGCTGTT AGAATAGCAA 12960
CAGTGTACTC ATGGGCTTAC GGTGATGATG ATAGCTCTTG GAACGAAGCC TGGTTGTTGG 13020
CTAGGCAAAG GGCCAATGTG AGCCTGGAGG AGCTAAGGGT GATCACTCCC ATCTCAACTT 13080
CGACTAATTT AGCGCATAGG TTGAGGGATC GTAGCACTCA AGTGAAATAC TCAGGTACAT 13140
CCCTTGTCCG AGTGGCGAGG TATACCACAA TCTCCAACGA CAATCTCTCA TTTGTCATAT 13200
CAGATAAGAA GGTTGATACT AACTTTATAT ACCAACAAGG AATGCTTCTA GGGTTGGGTG 13260
TTTTAGAAAC ATTGTTTCGA CTCGAGAAAG ATACCGGATC ATCTAACACG GTATTACATC 13320
TTCACGTCGA AACAGATTGT TGCGTGATCC CGATGATAGA TCATCCCAGG ATACCCAGCT 13380
CCCGCAAGCT AGAGCTGAGG GCAGAGCTAT GTACCAACCC ATTGATATAT GATAATGCAC 13440
CTTTAATTGA CAGAGATGCA ACAAGGCTAT ACACCCAGAG CCATAGGAGG CACCTTGTGG 13500
AATTTGTTAC ATGGTCCACA CCCCAACTAT ATCACATTTT AGCTAAGTCC ACAGCACTAT 13560
CTATGATTGA CCTGGTAACA AAATTTGAGA AGGACCATAT GAATGAAATT TCAGCTCTCA 13620
TAGGGGATGA CGATATCAAT AGTTTCATAA CTGAGTTTCT GCTCATAGAG CCAAGATTAT 13680
TCACTATCTA CTTGGGCCAG TGTGCGGCCA TCAATTGGGC ATTTGATGTA CATTATCATA 13740
GACCATCAGG GAAATATCAG ATGGGTGAGC TGTTGTCATC GTTCCTTTCT AGAATGAGCA 13800

AAGGAGTGTT TAAGGTGCTT GTCAATGCTC TAAGCCACCC AAAGATCTAC AAGAAATTCT 13860

GGCATTGTGG TATTATAGAG CCTATCCATG GTCCTTCACT TGATGCTCAA AACTTGCACA 13920

CAACTGTGTG CAACATGGTT TACACATGCT ATATGACCTA CCTCGACCTG TTGTTGAATG 13980

AAGAGTTAGA AGAGTTCACA TTTCTCTTGT GTGAAAGCGA CGAGGATGTA GTACCGGACA 14040

GATTCGACAA CATCCAGGCA AAACACTTAT GTGTTCTGGC AGATTTGTAC TGTCAACCAG 14100

GGACCTGCCC ACCAATTCGA GGTCTAAGAC CGGTAGAGAA ATGTGCAGTT CTAACCGACC 14160

ATATCAAGGC AGAGGCTAGG TTATCTCCAG CAGGATCTTC GTGGAACATA AATCCAATTA 14220

TTGTAGACCA TTACTCATGC TCTCTGACTT ATCTCCGGCG AGGATCGATC AAACAGATAA 14280

GATTGAGAGT TGATCCAGGA TTCATTTTCG ACGCCCTCGC TGAGGTAAAT GTCAGTCAGC 14340

CAAAGATCGG CAGCAACAAC ATCTCAAATA TGAGCATCAA GGATTTCAGA CCCCCACACG 14400

ATGATGTTGC AAAATTGCTC AAAGATATCA ACACAAGCAA GCACAATCTT CCCATTTCAG 14460

GGGGCAATCT CGCCAATTAT GAAATCCATG CTTTCCGCAG AATCGGGTTG AACTCATCTG 14520

CTTGCTACAA AGCTGTTGAG ATATCAACAT TAATTAGGAG ATGCCTTGAG CCAGGGGAAG 14580

ACGGCTTGTT CTTGGGTGAG GGATCGGGTT CTATGTTGAT CACTTATAAG GAGATACTTA 14640

AACTAAACAA GTGCTTCTAT AATAGTGGGG TTTCCGCCAA TTCTAGATCT GGTCAAAGGG 14700

AATTAGCACC CTATCCCTCC GAAGTTGGCC TTGTCGAACA CAGAATGGGA GTAGGTAATA 14760

TTGTCAAAGT GCTCTTTAAC GGGAGGCCCG AAGTCACGTG GGTAGGCAGT GTAGATTGCT 14820

TCAATTTCAT AGTTAGTAAT ATCCCTACCT CTAGTGTGGG GTTTATCCAT TCAGATATAG 14880

AGACCTTGCC TAACAAAGAT ACTATAGAGA AGCTAGAGGA ATTGGCAGCC ATCTTATCGA 14940

TGGCTCTGCT CCTGGGCAAA ATAGGATCAA TACTGGTGAT TAAGCTTATG CCTTTCAGCG 15000

GGGATTTTGT TCAGGGATTT ATAAGTTATG TAGGGTCTCA TTATAGAGAA GTGAACCTTG 15060

TATACCCTAG ATACAGCAAC TTCATATCTA CTGAATCTTA TTTGGTTATG ACAGATCTCA 15120

AGGCTAACCG GCTAATGAAT CCTGAAAAGA TTAAGCAGCA GATAATTGAA TCATCTGTGA 15180

GGACTTCACC TGGACTTATA GGTCACATCC TATCCATTAA GCAACTAAGC TGCATACAAG 15240

CAATTGTGGG AGACGCAGTT AGTAGAGGTG ATATCAATCC TACTCTGAAA AAACTTACAC 15300

CTATAGAGCA GGTGCTGATC AATTGCGGGT TGGCAATTAA CGGACCTAAG CTGTGCAAAG 15360

AATTGATCCA CCATGATGTT GCCTCAGGGC AAGATGGATT GCTTAATTCT ATACTCATCC 15420

TCTACAGGGA GTTGGCAAGA TTCAAAGACA ACCAAAGAAG TCAACAAGGG ATGTTCCACG 15480

CTTACCCCGT ATTGGTAAGT AGCAGGCAAC GAGAACTTAT ATCTAGGATC ACCCGCAAAT 15540

TTTGGGGGCA CATTCTTCTT TACTCCGGGA ACAGAAAGTT GATAAATAAG TTTATCCAGA 15600

ATCTCAAGTC CGGCTATCTG ATACTAGACT TACACCAGAA TATCTTCGTT AAGAATCTAT 15660

CCAAGTCAGA GAAACAGATT ATTATGACGG GGGGTTTGAA ACGTGAGTGG GTTTTTAAGG 15720

TAACAGTCAA GGAGACCAAA GAATGGTATA AGTTAGTCGG ATACAGTGCC CTGATTAAGG 15780

ACTAATTGGT TGAACTCCGG AACCCTAATC CTGCCCTAGG TGGTTAGGCA TTATTTGCAA 15840

TATATTAAAG AAAACTTTGA AAATACGAAG TTTCTATTCC CAGCTTTGTC TGGT 15894

(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2183 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

Met Asp Ser Leu Ser Val Asn Gln Ile Leu Tyr Pro Glu Val His Leu
1 5 10 15

Asp Ser Pro Ile Val Thr Asn Lys Ile Val Ala Ile Leu Glu Tyr Ala
20 25 30

Arg Val Pro His Ala Tyr Ser Leu Glu Asp Pro Thr Leu Cys Gln Asn
35 40 45

Ile Lys His Arg Leu Lys Asn Gly Phe Ser Asn Gln Met Ile Ile Asn
50 55 60

Asn Val Glu Val Gly Asn Val Ile Lys Ser Lys Leu Arg Ser Tyr Pro
65 70 75 80

Ala His Ser His Ile Pro Tyr Pro Asn Cys Asn Gln Asp Leu Phe Asn
85 90 95

Ile Glu Asp Lys Glu Ser Thr Arg Lys Ile Arg Glu Leu Leu Lys Lys
100 105 110

Gly Asn Ser Leu Tyr Ser Lys Val Ser Asp Lys Val Phe Gln Cys Leu
115 120 125

Arg Asp Thr Asn Ser Arg Leu Gly Leu Gly Ser Glu Leu Arg Glu Asp
130 135 140

Ile Lys Glu Lys Val Ile Asn Leu Gly Val Tyr Met His Ser Ser Gln
145 150 155 160

Trp Phe Glu Pro Phe Leu Phe Trp Phe Thr Val Lys Thr Glu Met Arg
165 170 175

Ser Val Ile Lys Ser Gln Thr His Thr Cys His Arg Arg Arg His Thr
180 185 190

Pro Val Phe Phe Thr Gly Ser Ser Val Glu Leu Leu Ile Ser Arg Asp
195 200 205

Leu Val Ala Ile Ile Ser Lys Glu Ser Gln His Val Tyr Tyr Leu Thr
210 215 220

Phe Glu Leu Val Leu Met Tyr Cys Asp Val Ile Glu Gly Arg Leu Met
225 230 235 240

Thr Glu Thr Ala Met Thr Ile Asp Ala Arg Tyr Thr Glu Leu Leu Gly
245 250 255

Arg Val Arg Tyr Met Trp Lys Leu Ile Asp Gly Phe Phe Pro Ala Leu
260 265 270

Gly Asn Pro Thr Tyr Gln Ile Val Ala Met Leu Glu Pro Leu Ser Leu
275 280 285

Ala Tyr Leu Gln Leu Arg Asp Ile Thr Val Glu Leu Arg Gly Ala Phe
290 295 300

Leu Asn His Cys Phe Thr Glu Ile His Asp Val Leu Asp Gln Asn Gly
305 310 315 320

Phe Ser Asp Glu Gly Thr Tyr His Glu Leu Ile Glu Ala Leu Asp Tyr
325 330 335

Ile Phe Ile Thr Asp Asp Ile His Leu Thr Gly Glu Ile Phe Ser Phe
340 345 350

Phe Arg Ser Phe Gly His Pro Arg Leu Glu Ala Val Thr Ala Ala Glu
355 360 365

Asn Val Arg Lys Tyr Met Asn Gln Pro Lys Val Ile Val Tyr Glu Thr

370 375 380

Leu Met Lys Gly His Ala Ile Phe Cys Gly Ile Ile Ile Asn Gly Tyr
385 390 395 400

Arg Asp Arg His Gly Gly Ser Trp Pro Pro Leu Thr Leu Pro Leu His
405 410 415

Ala Ala Asp Thr Ile Arg Asn Ala Gln Ala Ser Gly Glu Gly Leu Thr
420 425 430

His Glu Gln Cys Val Asp Asn Trp Lys Ser Phe Ala Gly Val Lys Phe
435 440 445

Gly Cys Phe Met Pro Leu Ser Leu Asp Ser Asp Leu Thr Met Tyr Leu
450 455 460

Lys Asp Lys Ala Leu Ala Ala Leu Gln Arg Glu Trp Asp Ser Val Tyr
465 470 475 480

Pro Lys Glu Phe Leu Arg Tyr Asp Pro Pro Lys Gly Thr Gly Ser Arg
485 490 495

Arg Leu Val Asp Val Phe Leu Asn Asp Ser Ser Phe Asp Pro Tyr Asp
500 505 510

Val Ile Met Tyr Val Val Ser Gly Ala Tyr Leu His Asp Pro Glu Phe
515 520 525

Asn Leu Ser Tyr Ser Leu Lys Glu Lys Glu Ile Lys Glu Thr Gly Arg
530 535 540

Leu Phe Ala Lys Met Thr Tyr Lys Met Arg Ala Cys Gln Val Ile Ala
545 550 555 560

Glu Asn Leu Ile Ser Asn Gly Ile Gly Lys Tyr Phe Lys Asp Asn Gly
565 570 575

Met Ala Lys Asp Glu His Asp Leu Thr Lys Ala Leu His Thr Leu Ala
580 585 590

Val Ser Gly Val Pro Lys Asp Leu Lys Glu Ser His Arg Gly Gly Pro
595 600 605

Val Leu Lys Thr Tyr Ser Arg Ser Pro Val His Thr Ser Thr Arg Asn
610 615 620

Val Arg Ala Ala Lys Gly Phe Ile Gly Phe Pro Gln Val Ile Arg Gln
625 630 635 640

Asp Gln Asp Thr Asp His Pro Glu Asn Met Glu Ala Tyr Glu Thr Val
645 650 655

Ser Ala Phe Ile Thr Thr Asp Leu Lys Lys Tyr Cys Leu Asn Trp Arg
660 665 670

Tyr Glu Thr Ile Ser Leu Phe Ala Gln Arg Leu Asn Glu Ile Tyr Gly
675 680 685

Leu Pro Ser Phe Phe Gln Trp Leu His Lys Arg Leu Glu Thr Ser Val
690 695 700

Leu Tyr Val Ser Asp Pro His Cys Pro Pro Asp Leu Asp Ala His Ile
705 710 715 720

Pro Leu Tyr Lys Val Pro Asn Asp Gln Ile Phe Ile Lys Tyr Pro Met
725 730 735

Gly Gly Ile Glu Gly Tyr Cys Gln Lys Leu Trp Thr Ile Ser Thr Ile
740 745 750

Pro Tyr Leu Tyr Leu Ala Ala Tyr Glu Ser Gly Val Arg Ile Ala Ser
755 760 765

Leu Val Gln Gly Asp Asn Gln Thr Ile Ala Val Thr Lys Arg Val Pro
770 775 780

Ser Thr Trp Pro Tyr Asn Leu Lys Lys Arg Glu Ala Ala Arg Val Thr
785 790 795 800

Arg Asp Tyr Phe Val Ile Leu Arg Gln Arg Leu His Asp Ile Gly His
805 810 815

His Leu Lys Ala Asn Glu Thr Ile Val Ser Ser His Phe Phe Val Tyr
820 825 830

Ser Lys Gly Ile Tyr Tyr Asp Gly Leu Leu Val Ser Gln Ser Leu Lys
835 840 845

Ser Ile Ala Arg Cys Val Phe Trp Ser Glu Thr Ile Val Asp Glu Thr
850 855 860

Arg Ala Ala Cys Ser Asn Ile Ala Thr Thr Met Ala Lys Ser Ile Glu
865 870 875 880

Arg Gly Tyr Asp Arg Tyr Leu Ala Tyr Ser Leu Asn Val Leu Lys Val
885 890 895

Ile Gln Gln Ile Leu Ile Ser Leu Gly Phe Thr Ile Asn Ser Thr Met
900 905 910

Thr Arg Asp Val Val Ile Pro Leu Leu Thr Asn Asn Asp Leu Leu Ile
915 920 925

Arg Met Ala Leu Leu Pro Ala Pro Ile Gly Gly Met Asn Tyr Leu Asn
930 935 940

Met Ser Arg Leu Phe Val Arg Asn Ile Gly Asp Pro Val Thr Ser Ser
945 950 955 960

Ile Ala Asp Leu Lys Arg Met Ile Leu Ala Ser Leu Met Pro Glu Glu
965 970 975

Thr Leu His Gln Val Met Thr Gln Gln Pro Gly Asp Ser Ser Phe Leu
980 985 990

Asp Trp Ala Ser Asp Pro Tyr Ser Ala Asn Leu Val Cys Val Gln Ser
995 1000 1005

Ile Thr Arg Leu Leu Lys Asn Ile Thr Ala Arg Phe Val Leu Ile His
1010 1015 1020

Ser Pro Asn Pro Met Leu Lys Gly Leu Phe His Asp Asp Ser Lys Glu
1025 1030 1035 1040

Glu Asp Glu Gly Leu Ala Ala Phe Leu Met Asp Arg His Ile Ile Val
1045 1050 1055

Pro Arg Ala Ala His Glu Ile Leu Asp His Ser Val Thr Gly Ala Arg
1060 1065 1070

Glu Ser Ile Ala Gly Met Leu Asp Thr Thr Lys Gly Leu Ile Arg Ala
1075 1080 1085

Ser Met Arg Lys Gly Gly Leu Thr Ser Arg Val Ile Thr Arg Leu Ser
1090 1095 1100

Asn Tyr Asp Tyr Glu Gln Phe Arg Ala Gly Met Val Leu Leu Thr Gly
1105 1110 1115 1120

Arg Lys Arg Asn Val Leu Ile Asp Lys Glu Ser Cys Ser Val Gln Leu
1125 1130 1135

Ala Arg Ala Leu Arg Ser His Met Trp Ala Arg Leu Ala Arg Gly Arg
1140 1145 1150

Pro Ile Tyr Gly Leu Glu Val Pro Asp Val Leu Glu Ser Met Arg Gly
1155 1160 1165

His Leu Ile Arg Arg His Glu Thr Cys Val Ile Cys Glu Cys Gly Ser
1170 1175 1180

Val Asn Tyr Gly Trp Phe Phe Val Pro Ser Gly Cys Gln Leu Asp Asp
1185 1190 1195 1200

Ile Asp Lys Glu Thr Ser Ser Leu Arg Val Pro Tyr Ile Gly Ser Thr

1205 1210 1215

Thr Asp Glu Arg Thr Asp Met Lys Leu Ala Phe Val Arg Ala Pro Ser
1220 1225 1230

Arg Ser Leu Arg Ser Ala Val Arg Ile Ala Thr Val Tyr Ser Trp Ala
1235 1240 1245

Tyr Gly Asp Asp Asp Ser Ser Trp Asn Glu Ala Trp Leu Leu Ala Arg
1250 1255 1260

Gln Arg Ala Asn Val Ser Leu Glu Glu Leu Arg Val Ile Thr Pro Ile
1265 1270 1275 1280

Ser Thr Ser Thr Asn Leu Ala His Arg Leu Arg Asp Arg Ser Thr Gln
1285 1290 1295

Val Lys Tyr Ser Gly Thr Ser Leu Val Arg Val Ala Arg Tyr Thr Thr
1300 1305 1310

Ile Ser Asn Asp Asn Leu Ser Phe Val Ile Ser Asp Lys Lys Val Asp
1315 1320 1325

Thr Asn Phe Ile Tyr Gln Gln Gly Met Leu Leu Gly Leu Gly Val Leu
1330 1335 1340

Glu Thr Leu Phe Arg Leu Glu Lys Asp Thr Gly Ser Ser Asn Thr Val
1345 1350 1355 1360

Leu His Leu His Val Glu Thr Asp Cys Cys Val Ile Pro Met Ile Asp
1365 1370 1375

His Pro Arg Ile Pro Ser Ser Arg Lys Leu Glu Leu Arg Ala Glu Leu
1380 1385 1390

Cys Thr Asn Pro Leu Ile Tyr Asp Asn Ala Pro Leu Ile Asp Arg Asp
1395 1400 1405

Ala Thr Arg Leu Tyr Thr Gln Ser His Arg Arg His Leu Val Glu Phe
1410 1415 1420

Val Thr Trp Ser Thr Pro Gln Leu Tyr His Ile Leu Ala Lys Ser Thr
1425 1430 1435 1440

Ala Leu Ser Met Ile Asp Leu Val Thr Lys Phe Glu Lys Asp His Met
1445 1450 1455

Asn Glu Ile Ser Ala Leu Ile Gly Asp Asp Asp Ile Asn Ser Phe Ile
1460 1465 1470

Thr Glu Phe Leu Leu Ile Glu Pro Arg Leu Phe Thr Ile Tyr Leu Gly
1475 1480 1485

Gln Cys Ala Ala Ile Asn Trp Ala Phe Asp Val His Tyr His Arg Pro
1490 1495 1500

Ser Gly Lys Tyr Gln Met Gly Glu Leu Leu Ser Ser Phe Leu Ser Arg
1505 1510 1515 1520

Met Ser Lys Gly Val Phe Lys Val Leu Val Asn Ala Leu Ser His Pro
1525 1530 1535

Lys Ile Tyr Lys Lys Phe Trp His Cys Gly Ile Ile Glu Pro Ile His
1540 1545 1550

Gly Pro Ser Leu Asp Ala Gln Asn Leu His Thr Thr Val Cys Asn Met
1555 1560 1565

Val Tyr Thr Cys Tyr Met Thr Tyr Leu Asp Leu Leu Leu Asn Glu Glu
1570 1575 1580

Leu Glu Glu Phe Thr Phe Leu Leu Cys Glu Ser Asp Glu Asp Val Val
1585 1590 1595 1600

Pro Asp Arg Phe Asp Asn Ile Gln Ala Lys His Leu Cys Val Leu Ala
1605 1610 1615

Asp Leu Tyr Cys Gln Pro Gly Thr Cys Pro Pro Ile Arg Gly Leu Arg
1620 1625 1630

Pro Val Glu Lys Cys Ala Val Leu Thr Asp His Ile Lys Ala Glu Ala
1635 1640 1645

Arg Leu Ser Pro Ala Gly Ser Ser Trp Asn Ile Asn Pro Ile Ile Val
1650 1655 1660

Asp His Tyr Ser Cys Ser Leu Thr Tyr Leu Arg Arg Gly Ser Ile Lys
1665 1670 1675 1680

Gln Ile Arg Leu Arg Val Asp Pro Gly Phe Ile Phe Asp Ala Leu Ala
1685 1690 1695

Glu Val Asn Val Ser Gln Pro Lys Ile Gly Ser Asn Asn Ile Ser Asn
1700 1705 1710

Met Ser Ile Lys Asp Phe Arg Pro Pro His Asp Asp Val Ala Lys Leu
1715 1720 1725

Leu Lys Asp Ile Asn Thr Ser Lys His Asn Leu Pro Ile Ser Gly Gly
1730 1735 1740

Asn Leu Ala Asn Tyr Glu Ile His Ala Phe Arg Arg Ile Gly Leu Asn
1745 1750 1755 1760

Ser Ser Ala Cys Tyr Lys Ala Val Glu Ile Ser Thr Leu Ile Arg Arg
1765 1770 1775

Cys Leu Glu Pro Gly Glu Asp Gly Leu Phe Leu Gly Glu Gly Ser Gly
1780 1785 1790

Ser Met Leu Ile Thr Tyr Lys Glu Ile Leu Lys Leu Asn Lys Cys Phe
1795 1800 1805

Tyr Asn Ser Gly Val Ser Ala Asn Ser Arg Ser Gly Gln Arg Glu Leu
1810 1815 1820

Ala Pro Tyr Pro Ser Glu Val Gly Leu Val Glu His Arg Met Gly Val
1825 1830 1835 1840

Gly Asn Ile Val Lys Val Leu Phe Asn Gly Arg Pro Glu Val Thr Trp
1845 1850 1855

Val Gly Ser Val Asp Cys Phe Asn Phe Ile Val Ser Asn Ile Pro Thr
1860 1865 1870

Ser Ser Val Gly Phe Ile His Ser Asp Ile Glu Thr Leu Pro Asn Lys
1875 1880 1885

Asp Thr Ile Glu Lys Leu Glu Glu Leu Ala Ala Ile Leu Ser Met Ala
1890 1895 1900

Leu Leu Leu Gly Lys Ile Gly Ser Ile Leu Val Ile Lys Leu Met Pro
1905 1910 1915 1920

Phe Ser Gly Asp Phe Val Gln Gly Phe Ile Ser Tyr Val Gly Ser His
1925 1930 1935

Tyr Arg Glu Val Asn Leu Val Tyr Pro Arg Tyr Ser Asn Phe Ile Ser
1940 1945 1950

Thr Glu Ser Tyr Leu Val Met Thr Asp Leu Lys Ala Asn Arg Leu Met
1955 1960 1965

Asn Pro Glu Lys Ile Lys Gln Gln Ile Ile Glu Ser Ser Val Arg Thr
1970 1975 1980

Ser Pro Gly Leu Ile Gly His Ile Leu Ser Ile Lys Gln Leu Ser Cys
1985 1990 1995 2000

Ile Gln Ala Ile Val Gly Asp Ala Val Ser Arg Gly Asp Ile Asn Pro
2005 2010 2015

Thr Leu Lys Lys Leu Thr Pro Ile Glu Gln Val Leu Ile Asn Cys Gly
2020 2025 2030

Leu Ala Ile Asn Gly Pro Lys Leu Cys Lys Glu Leu Ile His His Asp

2035 2040 2045

Val Ala Ser Gly Gln Asp Gly Leu Leu Asn Ser Ile Leu Ile Leu Tyr
2050 2055 2060

Arg Glu Leu Ala Arg Phe Lys Asp Asn Gln Arg Ser Gln Gln Gly Met
2065 2070 2075 2080

Phe His Ala Tyr Pro Val Leu Val Ser Ser Arg Gln Arg Glu Leu Ile
2085 2090 2095

Ser Arg Ile Thr Arg Lys Phe Trp Gly His Ile Leu Leu Tyr Ser Gly
2100 2105 2110

Asn Arg Lys Leu Ile Asn Lys Phe Ile Gln Asn Leu Lys Ser Gly Tyr
2115 2120 2125

Leu Ile Leu Asp Leu His Gln Asn Ile Phe Val Lys Asn Leu Ser Lys
2130 2135 2140

Ser Glu Lys Gln Ile Ile Met Thr Gly Gly Leu Lys Arg Glu Trp Val
2145 2150 2155 2160

Phe Lys Val Thr Val Lys Glu Thr Lys Glu Trp Tyr Lys Leu Val Gly
2165 2170 2175

Tyr Ser Ala Leu Ile Lys Asp
2180

(2) INFORMATION FOR SEQ ID NO:3:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 15894 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

ACCAAACAAA GTTGGGTAAG GATAGATCAA TCAATGATCA TATTCTAGTA CACTTAGGAT 60

TCAAGATCCT ATTATCAGGG ACAAGAGCAG GATTAGGGAT ATCCGAGATG GCCACACTTC 120

TAAGGAGCTT AGCATTGTTC AAAAGAAACA AGGACAAACC ACCCATTACA TCAGGATCCG 180

GTGGAGCCAT CAGAGGAATC AAACACATTA TTATAGTACC AATCCCGGGA GATTCCTCAA 240

TTACCACTCG ATCTAGACTT CTGGACCGGT TGGTCAGGTT AATTGGAAAC CCGGATGTGA 300

GCGGGCCCAA ACTAACAGGG GCACTAATAG GTATATTATC CTTATTTGTG GAGTCTCCAG 360

GTCAATTGAT TCAGAGGATC ACCGATGACC CTGACGTTAG CATAAGGCTG TTAGAGGTTG 420

TCCAGAGTGA CCAGTCACAA TCTGGCCTTA CCTTCGCATC AAGAGGTACC AACATGGAGG 480

ATGAGGCGGA CCAATATTTT TCACATGATG ATCCAAGTAG TAGTGATCAA TCCAGGTTCG 540

GATGGTTCGA GAACAAGGAA ATCTCAGATA TTGAAGTGCA AGACCCTGAG GGATTCAACA 600

TGATTCTGGG TACCATCCTA GCTCAAATTT GGGTCTTGCT CGCAAAGGCG GTTACGGCCC 660

CAGACACGGC AGCTGATTCG GAGCTAAGAA GGTGGATAAA GTACACCCAA CAAAGAAGGG 720

TAGTTGGTGA ATTTAGATTG GAGAGAAAAT GGTTGGATGT GGTGAGGAAC AGGATTGCCG 780

AGGACCTCTC CTTACGCCGA TTCATGGTCG CTCTAATCCT GGATATCAAG AGAACACCCG 840

GGAACAAACC CAGGATTGCT GAAATGATAT GTGACATTGA TACATATATC GTAGAGGCAG 900

GATTAGCCAG TTTTATCCTG ACTATTAAGT TTGGGATAGA AACTATGTAT CCTGCTCTTG 960

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CCAAGTCAGA GAAACAGATT ATTATGACGG GGGGTTTGAA ACGTGAGTGG GTTTTTAAGG 15720

TAACAGTCAA GGAGACCAAG GAATGGTATA AGTTAGTCGG ATACAGTGCC CTGATTAAGG 15780

ACTAATTGGT TGAACTCCGG AACCCTAATC CTGCCCCAGG TGGTTAGGCA TTATTTGTAA 15840

TATATTAAAG AAAACTTTGA AAATACGAAG TTTCTATTCC CAGCTTTGTC TGGT 15894

(2) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2183 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

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Met Asp Ser Leu Ser Val Asn Gln Ile Leu Tyr Pro Glu Val His Leu
1               5                   10                  15

Asp Ser Pro Ile Val Thr Asn Lys Ile Val Ala Ile Leu Glu Tyr Ala
            20                  25                  30

Arg Val Pro His Ala Tyr Ser Leu Glu Asp Pro Thr Leu Cys Gln Asn
        35                  40                  45

Ile Lys His Arg Leu Lys Asn Gly Phe Ser Asn Gln Met Ile Ile Asn
    50                  55                  60

Asn Val Glu Val Gly Asn Val Ile Lys Ser Lys Leu Arg Ser Tyr Pro
65                  70                  75                  80

Ala His Ser His Ile Pro Tyr Pro Asn Cys Asn Gln Asp Leu Phe Asn
                85                  90                  95

Ile Glu Asp Lys Glu Ser Thr Arg Lys Ile Arg Glu Leu Leu Lys Lys
            100                 105                 110

Gly Asn Ser Leu Tyr Ser Lys Val Ser Asn Lys Val Phe Gln Cys Leu
        115                 120                 125

Arg Asp Thr Asn Ser Arg Leu Gly Leu Gly Ser Glu Leu Arg Glu Asp
    130                 135                 140

Ile Lys Glu Lys Val Ile Asn Leu Gly Val Tyr Met His Ser Ser Gln
145                 150                 155                 160

Trp Phe Glu Pro Phe Leu Phe Trp Phe Thr Val Lys Thr Glu Met Arg
                165                 170                 175

Ser Val Ile Lys Ser Gln Thr His Thr Cys His Arg Arg Arg His Thr
            180                 185                 190
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Pro Val Phe Phe Thr Gly Ser Ser Val Glu Leu Leu Ile Ser Arg Asp
        195                 200                 205

Leu Val Ala Ile Ile Ser Lys Glu Ser Gln His Val Tyr Tyr Leu Thr
    210                 215                 220

Phe Glu Leu Val Leu Met Tyr Cys Asp Val Ile Glu Gly Arg Leu Met
225                 230                 235                 240

Thr Glu Thr Ala Met Thr Ile Asp Ala Arg Tyr Thr Glu Leu Leu Gly
                245                 250                 255

Arg Val Arg Tyr Met Trp Lys Leu Ile Asp Gly Phe Phe Pro Ala Leu
            260                 265                 270

Gly Asn Pro Thr Tyr Gln Ile Val Ala Met Leu Glu Pro Leu Ser Leu
        275                 280                 285

Ala Tyr Leu Gln Leu Arg Asp Ile Thr Val Glu Leu Arg Gly Ala Phe
    290                 295                 300

Leu Asn His Cys Phe Thr Glu Ile His Asp Val Leu Asp Gln Asn Gly
305                 310                 315                 320

Phe Ser Asp Glu Gly Thr Tyr His Glu Leu Val Glu Ala Leu Asp Tyr
                325                 330                 335

Ile Phe Ile Thr Asp Asp Ile His Leu Thr Gly Glu Ile Phe Ser Phe
            340                 345                 350

Phe Arg Ser Phe Gly His Pro Arg Leu Glu Ala Val Thr Ala Ala Glu
        355                 360                 365

Asn Val Arg Lys Tyr Met Asn Gln Pro Lys Val Ile Val Tyr Glu Thr
    370                 375                 380

Leu Met Lys Gly His Ala Ile Phe Cys Gly Ile Ile Ile Asn Gly Tyr
385                 390                 395                 400

Arg Asp Arg His Gly Gly Ser Trp Pro Pro Leu Thr Leu Pro Leu His
                405                 410                 415

Ala Ala Asp Thr Ile Arg Asn Ala Gln Ala Ser Gly Glu Gly Leu Thr
            420                 425                 430

His Glu Gln Cys Val Asp Asn Trp Lys Ser Phe Ala Gly Val Lys Phe
        435                 440                 445

Gly Cys Phe Met Pro Leu Ser Leu Asp Ser Asp Leu Thr Met Tyr Leu
    450                 455                 460
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Lys Asp Lys Ala Leu Ala Ala Leu Gln Arg Glu Trp Asp Ser Val Tyr
465 470 475 480

Pro Lys Glu Phe Leu Arg Tyr Asp Pro Pro Lys Gly Thr Gly Ser Arg
485 490 495

Arg Leu Val Asp Val Phe Leu Asn Asp Ser Ser Phe Asp Pro Tyr Asp
500 505 510

Met Ile Met Tyr Val Val Ser Gly Ala Tyr Leu His Asp Pro Glu Phe
515 520 525

Asn Leu Ser Tyr Ser Leu Lys Glu Lys Glu Ile Lys Glu Thr Gly Arg
530 535 540

Leu Phe Ala Lys Met Thr Tyr Lys Met Arg Ala Cys Gln Val Ile Ala
545 550 555 560

Glu Asn Leu Ile Ser Asn Gly Ile Gly Lys Tyr Phe Lys Asp Asn Gly
565 570 575

Met Ala Lys Asp Glu His Asp Leu Thr Lys Ala Leu His Thr Leu Ala
580 585 590

Val Ser Gly Val Pro Lys Asp Leu Lys Glu Ser His Arg Gly Gly Pro
595 600 605

Val Leu Lys Thr Tyr Ser Arg Ser Pro Ala His Thr Asn Thr Arg Asn
610 615 620

Val Arg Ala Ala Lys Gly Phe Ile Gly Phe Pro Gln Ile Ile Arg Gln
625 630 635 640

Asp Gln Asp Thr Asn His Pro Glu Asn Met Glu Ala Tyr Glu Thr Val
645 650 655

Ser Ala Phe Ile Thr Thr Asp Leu Lys Lys Tyr Cys Leu Asn Trp Arg
660 665 670

Tyr Glu Thr Ile Ser Leu Phe Ala Gln Arg Leu Asn Glu Ile Tyr Gly
675 680 685

Leu Pro Ser Phe Phe Gln Trp Leu His Lys Arg Leu Glu Thr Ser Val
690 695 700

Leu Tyr Val Ser Asp Pro His Cys Pro Pro Asp Leu Asp Ala His Ile
705 710 715 720

Pro Leu Cys Lys Val Pro Asn Asp Gln Ile Phe Ile Lys Tyr Pro Met
725 730 735

Gly Gly Ile Glu Gly Tyr Cys Gln Lys Leu Trp Thr Ile Ser Thr Ile

740 745 750

Pro Tyr Leu Tyr Leu Ala Ala Tyr Glu Ser Gly Val Arg Ile Ala Ser
755 760 765

Leu Val Gln Gly Asp Asn Gln Thr Ile Ala Val Thr Lys Arg Val Pro
770 775 780

Ser Thr Trp Pro Tyr Asn Leu Lys Lys Trp Glu Ala Ala Arg Val Thr
785 790 795 800

Arg Asp Tyr Phe Val Ile Leu Arg Gln Arg Leu His Asp Ile Gly His
805 810 815

His Leu Lys Ala Asn Glu Thr Ile Val Ser Ser His Phe Phe Val Tyr
820 825 830

Ser Lys Gly Ile Tyr Tyr Asp Gly Leu Leu Val Ser Gln Ser Leu Lys
835 840 845

Ser Ile Ala Arg Cys Val Phe Trp Ser Glu Thr Ile Val Asp Glu Thr
850 855 860

Arg Ala Ala Cys Ser Asn Ile Ala Thr Thr Met Ala Lys Ser Ile Glu
865 870 875 880

Arg Gly Tyr Asp Arg Tyr Leu Ala Tyr Ser Leu Asn Val Leu Lys Val
885 890 895

Ile Gln Gln Ile Leu Ile Ser Leu Gly Phe Thr Ile Asn Ser Thr Met
900 905 910

Thr Gln Asp Val Val Ile Pro Leu Leu Thr Asn Asn Asp Leu Leu Ile
915 920 925

Arg Met Ala Leu Leu Pro Ala Pro Ile Gly Gly Met Asn Tyr Leu Asn
930 935 940

Met Ser Arg Leu Phe Val Arg Asn Ile Gly Asp Pro Val Thr Ser Ser
945 950 955 960

Ile Ala Asp Leu Lys Arg Met Ile Leu Ala Ser Leu Met Pro Glu Glu
965 970 975

Thr Leu His Gln Val Met Thr Gln Gln Pro Gly Asp Ser Ser Phe Leu
980 985 990

Asp Trp Ala Ser Asp Pro Tyr Ser Ala Asn Leu Val Cys Val Gln Ser
995 1000 1005

Ile Thr Arg Leu Leu Lys Asn Ile Thr Ala Arg Phe Val Leu Ile His
1010 1015 1020

Ser Pro Asn Pro Met Leu Lys Gly Leu Phe His Asp Asp Ser Lys Glu
1025 1030 1035 1040

Glu Asp Glu Gly Leu Ala Ala Phe Leu Met Asp Arg His Ile Ile Val
1045 1050 1055

Pro Arg Ala Ala His Glu Ile Leu Asp His Ser Val Thr Gly Ala Arg
1060 1065 1070

Glu Ser Ile Ala Gly Met Leu Asp Thr Thr Lys Gly Leu Ile Arg Ala
1075 1080 1085

Ser Met Arg Lys Gly Gly Leu Thr Ser Arg Val Ile Thr Arg Leu Ser
1090 1095 1100

Asn Tyr Asp Tyr Glu Gln Phe Arg Ala Gly Met Val Leu Leu Thr Gly
1105 1110 1115 1120

Arg Lys Arg Asn Val Leu Ile Asp Lys Glu Ser Cys Ser Val Gln Leu
1125 1130 1135

Ala Arg Ala Leu Arg Ser His Met Trp Ala Arg Leu Ala Arg Gly Arg
1140 1145 1150

Pro Ile Tyr Gly Leu Glu Val Pro Asp Val Leu Glu Ser Met Arg Gly
1155 1160 1165

His Leu Ile Arg Arg His Glu Thr Cys Val Ile Cys Glu Cys Gly Ser
1170 1175 1180

Val Asn Tyr Gly Trp Phe Phe Val Pro Ser Gly Cys Gln Leu Asp Asp
1185 1190 1195 1200

Ile Asp Lys Glu Thr Ser Ser Leu Arg Val Pro Tyr Ile Gly Ser Thr
1205 1210 1215

Thr Asp Glu Arg Thr Asp Met Lys Leu Ala Phe Val Arg Ala Pro Ser
1220 1225 1230

Arg Ser Leu Arg Ser Ala Val Arg Ile Ala Thr Val Tyr Ser Trp Ala
1235 1240 1245

Tyr Gly Asp Asp Asp Ser Ser Trp Asn Glu Ala Trp Leu Leu Ala Arg
1250 1255 1260

Gln Arg Ala Asn Val Ser Leu Glu Glu Leu Arg Val Ile Thr Pro Ile
1265 1270 1275 1280

Ser Thr Ser Thr Asn Leu Ala His Arg Leu Arg Asp Arg Ser Thr Gln
1285 1290 1295

Val Lys Tyr Ser Gly Thr Ser Leu Val Arg Val Ala Arg Tyr Thr Thr
1300 1305 1310

Ile Ser Asn Asp Asn Leu Ser Phe Val Ile Ser Asp Lys Lys Val Asp
1315 1320 1325

Thr Asn Phe Ile Tyr Gln Gln Gly Met Leu Leu Gly Leu Gly Val Leu
1330 1335 1340

Glu Thr Leu Phe Arg Leu Glu Lys Asp Thr Gly Ser Ser Asn Thr Val
1345 1350 1355 1360

Leu His Leu His Val Glu Thr Asp Cys Cys Val Ile Pro Met Ile Asp
1365 1370 1375

His Pro Arg Ile Pro Ser Ser Arg Lys Leu Glu Leu Arg Ala Glu Leu
1380 1385 1390

Cys Thr Asn Pro Leu Ile Tyr Asp Asn Ala Pro Leu Ile Asp Arg Asp
1395 1400 1405

Ala Thr Arg Leu Tyr Thr Gln Ser His Arg Arg His Leu Val Glu Phe
1410 1415 1420

Val Thr Trp Ser Thr Pro Gln Leu Tyr His Ile Leu Ala Lys Ser Thr
1425 1430 1435 1440

Ala Leu Ser Met Ile Asp Leu Val Thr Lys Phe Glu Lys Asp His Met
1445 1450 1455

Asn Glu Ile Ser Ala Leu Ile Gly Asp Asp Asp Ile Asn Ser Phe Ile
1460 1465 1470

Thr Glu Phe Leu Leu Ile Glu Pro Arg Leu Phe Thr Ile Tyr Leu Gly
1475 1480 1485

Gln Cys Ala Ala Ile Asn Trp Ala Phe Asp Val His Tyr His Arg Pro
1490 1495 1500

Ser Gly Lys Tyr Gln Met Gly Glu Leu Leu Ser Ser Phe Leu Ser Arg
1505 1510 1515 1520

Met Ser Lys Gly Val Phe Lys Val Leu Val Asn Ala Leu Ser His Pro
1525 1530 1535

Lys Ile Tyr Lys Lys Phe Trp His Cys Gly Ile Ile Glu Pro Ile His
1540 1545 1550

Gly Pro Ser Leu Asp Ala Gln Asn Leu His Thr Thr Val Cys Asn Met
1555 1560 1565

Val Tyr Thr Cys Tyr Met Thr Tyr Leu Asp Leu Leu Leu Asn Glu Glu

1570 1575 1580

Leu Glu Glu Phe Thr Phe Leu Leu Cys Glu Ser Asp Glu Asp Val Val
1585 1590 1595 1600

Pro Asp Arg Phe Asp Asn Ile Gln Ala Lys His Leu Cys Val Leu Ala
1605 1610 1615

Asp Leu Tyr Cys Gln Pro Gly Thr Cys Pro Pro Ile Arg Gly Leu Arg
1620 1625 1630

Pro Val Glu Lys Cys Ala Val Leu Thr Asp His Ile Lys Ala Glu Ala
1635 1640 1645

Arg Leu Ser Pro Ala Gly Ser Ser Trp Asn Ile Asn Pro Ile Ile Val
1650 1655 1660

Asp His Tyr Ser Cys Ser Leu Thr Tyr Leu Arg Arg Gly Ser Ile Lys
1665 1670 1675 1680

Gln Ile Arg Leu Arg Val Asp Pro Gly Phe Ile Phe Asp Ala Leu Ala
1685 1690 1695

Glu Val Asn Val Ser Gln Pro Lys Ile Gly Ser Asn Asn Ile Ser Asn
1700 1705 1710

Met Ser Ile Lys Asp Phe Arg Pro Pro His Asp Asp Val Ala Lys Leu
1715 1720 1725

Leu Lys Asp Ile Asn Thr Ser Lys His Asn Leu Pro Ile Ser Gly Gly
1730 1735 1740

Asn Leu Ala Asn Tyr Glu Ile His Ala Phe Arg Arg Ile Gly Leu Asn
1745 1750 1755 1760

Ser Ser Ala Cys Tyr Lys Ala Val Glu Ile Ser Thr Leu Ile Arg Arg
1765 1770 1775

Cys Leu Glu Pro Gly Glu Asp Gly Leu Phe Leu Gly Glu Gly Ser Gly
1780 1785 1790

Ser Met Leu Ile Thr Tyr Lys Glu Ile Leu Lys Leu Asn Lys Cys Phe
1795 1800 1805

Tyr Asn Ser Gly Val Ser Ala Asn Ser Arg Ser Gly Gln Arg Glu Leu
1810 1815 1820

Ala Pro Tyr Pro Ser Glu Val Gly Leu Val Glu His Arg Met Gly Val
1825 1830 1835 1840

Gly Asn Ile Val Lys Val Leu Phe Asn Gly Arg Pro Glu Val Thr Trp
1845 1850 1855

Val Gly Ser Val Asp Cys Phe Asn Tyr Ile Val Ser Asn Ile Pro Thr
1860 1865 1870

Ser Ser Val Gly Phe Ile His Ser Asp Ile Glu Thr Leu Pro Asn Lys
1875 1880 1885

Asp Thr Ile Glu Lys Leu Glu Glu Leu Ala Ala Ile Leu Ser Met Ala
1890 1895 1900

Leu Leu Leu Gly Lys Ile Gly Ser Ile Leu Val Ile Lys Leu Met Pro
1905 1910 1915 1920

Phe Ser Gly Asp Phe Val Gln Gly Phe Ile Ser Tyr Val Gly Ser His
1925 1930 1935

Tyr Arg Glu Val Asn Leu Val Tyr Pro Arg Tyr Ser Asn Phe Ile Ser
1940 1945 1950

Thr Glu Ser Tyr Leu Val Met Thr Asp Leu Lys Ala Asn Arg Leu Met
1955 1960 1965

Asn Pro Glu Lys Ile Lys Gln Gln Ile Ile Glu Ser Ser Val Arg Thr
1970 1975 1980

Ser Pro Gly Leu Ile Gly His Ile Leu Ser Ile Lys Gln Leu Ser Cys
1985 1990 1995 2000

Ile Gln Ala Ile Val Gly Asp Ala Val Ser Arg Gly Asp Ile Asn Pro
2005 2010 2015

Thr Leu Lys Lys Leu Thr Pro Ile Glu Gln Val Leu Ile Asn Cys Gly
2020 2025 2030

Leu Ala Ile Asn Gly Pro Lys Leu Cys Lys Glu Leu Ile His His Asp
2035 2040 2045

Val Ala Ser Gly Gln Asp Gly Leu Leu Asn Ser Ile Leu Ile Leu Tyr
2050 2055 2060

Arg Glu Leu Ala Arg Phe Lys Asp Asn Gln Arg Ser Gln Gln Gly Met
2065 2070 2075 2080

Phe His Ala Tyr Pro Val Leu Val Ser Ser Arg Gln Arg Glu Leu Ile
2085 2090 2095

Ser Arg Ile Thr Arg Lys Phe Trp Gly His Ile Leu Leu Tyr Ser Gly
2100 2105 2110

Asn Arg Lys Leu Ile Asn Lys Phe Ile Gln Asn Leu Lys Ser Gly Tyr
2115 2120 2125

Leu Ile Leu Asp Leu His Gln Asn Ile Phe Val Lys Asn Leu Ser Lys
2130 2135 2140

Ser Glu Lys Gln Ile Ile Met Thr Gly Gly Leu Lys Arg Glu Trp Val
2145 2150 2155 2160

Phe Lys Val Thr Val Lys Glu Thr Lys Glu Trp Tyr Lys Leu Val Gly
2165 2170 2175

Tyr Ser Ala Leu Ile Lys Asp
2180

(2) INFORMATION FOR SEQ ID NO:5:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 15894 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

ACCAAACAAA GTTGGGTAAG GATAGATCAA TCAATGATCA TATTCTAGTA CACTTAGGAT 60

TCAAGATCCT ATTATCAGGG ACAAGAGCAG GATTAGGGAT ATCCGAGATG GCCACACTTT 120

TAAGGAGCTT AGCATTGTTC AAAAGAAACA AGGACAAACC ACCCATTACA TCAGGATCCG 180

GTGGAGCCAT CAGAGGAATC AAACACATTA TTATAGTACC AATCCCTGGA GATTCCTCAA 240

TTACCACTCG ATCCAGACTA CTGGACCGGT TGGTCAGGTT AATTGGAAAC CCGGATGTGA 300

GCGGGCCCAA ACTAACAGGG GCACTAATAG GTATATTATC CTTGTTTGTG GAGTCTCCAG 360

GTCAATTGAT TCAGAGGATC ACCGATGACC CTGACGTTAG CATCAGGCTG TTAGAGGTTG 420

TCCAGAGTGA CCAGTCACAA TCTGGCCTTA CCTTCGCATC AAGAGGTACC AACATGGAGG 480

ATGAGGCGGA CCAATACTTT TCACATGATG ATCCAAGTAG TAGTGATCAA TCCAGGTCCG 540

GATGGTTCGA GAACAAGGAA ATCTCAGATA TTGAAGTGCA AGACCCTGAG GGATTCAACA 600

TGATTCTGGG TACCATTCTA GCCCAAATTT GGGTCTTGCT CGCGAAGGCG GTTACGGCCC 660

CAGACACGGC AGCTGATTCG GAGCTAAGAA GGTGGATAAA GTACACCCAA CAAAGAAGGG 720

TAGTTGGTGA ATTCAGATTG GAGAGAAAAT GGTTGGATGT GGTGAGGAAC AGGATTGCCG 780

AGGACCTCTC CTTACGCCGA TTCATGGTCG CTCTAATCCT GGATATCAAG AGGACACCCG 840

GGAACAAACC AAGGATTGCT GAAATGATAT GTGACATTGA TACATATATC GTAGAGGCAG 900

GATTAGCCAG TTTTATCCTA ACTATTAAGT TTGGGATAGA AACTATGTAT CCTGCTCTTG 960

GACTGCATGA ATTTGCTGGT GAGTTATCCA CACTTGAGTC CTTGATGAAT CTTTACCAGC 1020

AAATGGGAGA AACTGCACCC TACATGGTAA TCCTGGAGAA CTCAATTCAG AACAAGTTCA 1080

GTGCAGGATC ATACCCCCTG CTCTGGAGCT ATGCCATGGG AGTAGGGGTG GAACTTGAAA 1140

ACTCCATGGG AGGTTTGAAC TTTGGTCGAT CTTACTTTGA TCCAGCATAT TTTAGATTAG 1200

GGCAAGAGAT GGTGAGGAGG TCAGCTGGGA AAGTCAGTTC CACATTAGCA TCTGAACTCG 1260

GTATCACTGC TGAGGATGCA AGGCTTGTTT CAGAGATTGC AATGCACACT ACTGAGGACA 1320

GGACCAGTAG AGCGGTTGGA CCCAGACAAG CCCAAGTGTC ATTTCTACAC GGTGATCAAA 1380

GTGAGAATGA GCTACCAGGA TTGGGGGGCA AGGAAGATAG GAGGGTCAAA CAGAGTCGGG 1440

GAGAAGCCAG GGAGAGCTAC AGAGAAACCG GGTCTAGCAG AGCAAGCGAT GCGAGAGCTG 1500

CCCATCTTCC AACCAGCGCA CCCCTAGACA TTGACACTGC ATCGGAGTCA GGCCAAGATC 1560

CGCAGGACAG TCGACGGTCA GCTGACGCCC TGCTCAGGCT GCAAGCCATG GCAGGAATCT 1620

TGGAAGAACA AGGCTCAGAC ACGGACACCC CTAGGGTGTA CAATGACAGA GATCTTCTAG 1680

ACTAGGTGCG AGAGGCCGAG GACCAGAACA ACATCCGCCT ACCCTCCATC ATTGTTATAA 1740

AAAACTTAGG AACCAGGTCC ACACAGCCGC CAGCCAACCA ACCATCCACT CCTACGACTG 1800

GGGCCGATGG CAGAAGAGCA GGCACGCCAT GTCAAAAACG GACTGGAATG CATCCGGGCT 1860

CTCAAGGCCG AGCCCATCGG CTCACTGGCC GTCGAGGAAG CCATGGCAGC ATGGTCACAA 1920

ATATCAGACA ACCCAGGACA GGACCGAACC ACCCGCAAGG AAGAGGAGGC AGGCAGTTCG 1980

GGTCTCAGCA AACCATGCCT CTCAGCAATT GGATCAACTG AAGGCAGTGC ACCTCGCATC 2040

TGCGGTCAGG GATCTGGAGA GAGCGATGAC AACGCTGAAA CTTTGGGAAT CCCCTCAAGA 2100

AATCTCCAGG CATCAAGCAC TGGGTTACAG TGTTATCATG TTTATGATCA CAGCGGTGAA 2160

GCGGTTAAGG GAATCCAAGA TGCTGACTCT ATCATGGTTC AATCAGGCCT TGATGGTGAT 2220

AGCACCCTCT CAGGAGGAGA CGATGAATCT GAAAACAGCG ATGTGGATAT TGGCGAACCT 2280

GATACCGAGG GATATGCTAT CACTGACCGG GGATCTGCTC CCATCTCTAT GGGGTTCAGG 2340

GCTTCTGATG TTGAAACTGC AGAAGGAGGG GAGATCCACG AGCTCCTGAG ACTCCAATCT 2400

AGAGGCAACA ACTTCCCGAA GCTTGGGAAA ACTCTCAATG TTCCTCCGCC CCCGAACCCC 2460

GGTAGGGCCA GCACTTCCGA GACACCCATT AAAAAGGGGA CAGACGCGAG ATTAGCCTCA 2520

TTTGGAGCGG AGATCGCGTC TTTATTGACA GGTGGTGCAA CCCAATGTGC TCGAAAGTCA 2580

CCCTCGGAAC CATCAGGGCC AGGTGCACCT GTGGGGAATG TCCCCGAGTG TGTGAGCAAT 2640

GCCGCACTGA TACAGGAGTG GACACCCGAA TCTGGTACCA CAATCTCCCC GAGATCCCAG 2700

AATAATGAAG AAGGGGGAGA TTATTATGAT GATGAGCTGT TCTCCGATGT CCAAGACATC 2760

AAAACAGCCT TGGCCAAAAT ACACGAGGAT AATCAGAAGA TAATCTCCAA GCTAGAATCA 2820

CTGCTGTTAT TGAAGGGAGA AGTTGAGTCA ATTAAAAAGC AGATCAACAG GCAAAATATC 2880

AGCATATCCA CCCTGGAAGG ACACCTCTCA AGCATCATGA TCGCCATTCC TGGACTTGGG 2940

AAGGATCCCA ACGACCCCAC TGCAGATGTC GAACTCAATC CCGACCTGAA ACCCATCATA 3000

GGCAGAGATT CAGGCCGAGC ACTGGCCGAA GTTCTCAAGA AACCCGTTGC CAGCCGACAA 3060

CTCCAAGGAA TGACAAATGG ACGGACCAGT TCCAGAGGAC AGCTGCTGAA GGAATTTCAA 3120

CTAAAGCCGA TCGGGAAAAA GATGAGCTCA GCCGTCGGGT TTGTTCCTGA CACCGGCCCC 3180

GCATCACGCA GTGTAATCCG CTCCATTATA AAATCCAGCC GGCTAGAGGA GGATCGGAAG 3240

CGTTACCTGA TGACTCTCCT TGATGATATC AAAGGAGCCA ACGATCTTGC CAAGTTCCAC 3300

CAGATGCTGA TGAAGATAAT AATGAAGTAG CTACAGCTCA ACTTACCTGC CAACCTCATG 3360

CCAATCGACC TAATTAGTAC AGCCTAAATC CATTATAAAA AACTTAGGAG CAAAGTGATT 3420

GCCTCCCAAG TTCCACAATG ACAGAGATCT ACGACTTCGA CAAGTCGGCA TGGGACATCA 3480

AAGGGTCGAT CGCTCCGATA CAACCTACCA CCTACAGTGA TGGCAGGCTG GTGCCCCAGG 3540

TCAGAGTCAT AGATCCTGGT CTAGGCGACA GGAAGGATGA ATGCTTTACG TACATGTTTC 3600

TGCTGGGGGT TGTTGAGGAC AGCGATCCCC TAGGGCCTCC AATCGGGCGA GCATTTGGGT 3660

CCCTGCCCTT AGGTGTTGGT AGATCCACAG CAAAACCCGA AGAACTCCTC AAAGAGGCCA 3720

CTGAGCTTGA CATAGTCGTT AGACGTACAG CAGGGCTCAA TGAAAAACTG GTGTTCTACA 3780

ACAACACCCC ACTAACTCTC CTCACACCTT GGAGAAAGGT CCTAACAACA GGGAGTGTCT 3840

TCAACGCAAA CCAAGTGTGC AATGCGGTTA ATCTGATACC GCTGGATACC CCGCAGAGGT 3900

TCCGTGTTGT TTATATGAGC ATCACCCGTC TTTCGGATAA CGGGTATTAC ACCGTTCCTA 3960

GAAGAATGCT AGAATTCAGA TCGGTCAATG CAGTGGCTTT CAACCTGCTG GTGACCCTTA 4020

GGATTGACAA AGCGATTGGC CCTGGGAAGA TCATCGATAA TGCAGAGCAA CTTCCTGAGG 4080

CAACATTTAT GGTCCACATC GGGAACTTCA GGAGAAAGAA GAGTGAAGTC TACTCTGCTG 4140

ATTATTGCAA AATGAAAATC GAAAAGATGG GCCTGGTTTT TGCACTTGGT GGGATAGGGG 4200

GCACCAGTCT TCACATTAGA AGCACAGGCA AAATGAGCAA GACTCTCCAT GCACAACTCG 4260

GGTTCAAAAA GACCTTATGT TACCCACTGA TGGATATCAA TGAAGACCTT AATCGATTAC 4320

TCTGGAGGAG CAGATGCAAG ATAGTAAGAA TCCAGGCAGT TTTGCAGCCA TCAGTTCCCC 4380

AAGAATTCCG CATTTACGAC GACGTGATCA TAAATGATGA CCAAGGACTA TTCAAAGTTC 4440

TGTAGACCGT AGTGCCCAGC AATACCCGAA AACGACCCCC CTCATAATGA CAGCCAGAAG 4500

GCCCGGACAA AAAAGCCCCC TCCAAAAGAC TCCACGGACC AAGTGAGAGG CCAGCCAGCA 4560

GCTGACGGCA AGCGTGAACA CCAGGCGGCC TGGGCACAGA ACAGCCCCGA CACAAGGCAA 4620

CCACCAGCCA TCCCAATCTG CGTCCTCCTC GTGGGACCCC CGAGGACCAA CCCCCAAGGT 4680

CGCCCCCGAC CCAGACCACC AACCGCATCC CCACAGCCCC CGGGAAAGAG ACCCCCAGCA 4740

ACTGGAAGGC CCCTCCCCCT TTCCCTCAAC GCAAGAACTC CACAACCGAA CCGCACAAGC 4800

GATCGAGGTG ACCCAACCGC AGGCATCCGA CTCCCTAGAC AGATCCTCTC CCCCCGGCAA 4860

ACTAAACAAA ACTTAGGGCC AAGGAACATA CACACCCGAC AGAACCCAGA CCCCGGCCCA 4920

CGGCGCCGCG CCCCCACCTC CCGACAACCA GAGGGAGCCC CCAACCAATC CCGCCGGCTC 4980

CCCCGGTGCC CACAGGCAGG CACACCAACC CTCGAACAGA CCCAGCACCC AGCCATCGAC 5040

AATTCAAGAC GGGGGGCCCC CCCCAAAAAA AGGCCCCCAG GGGCCGACAG CCAGCACCGC 5100

GAGGAAGCCC ACCCACCCCA CACACGACCA CAGGAACCGA ACCAGAATCC AGACCACCCT 5160

GGGCCACCAG TTCCCAGACT CGGCCATCAC CCCGCAGAAA GGAAAGGCCA CAACCCGCGC 5220

ACCCCTGCCC TGATCCGGTG GGCGGCCACC CAACCCGAAC CAGCACCCAA GAGCGATCCC 5280

CGAAGGGCCC CCGAACCGCA AAAGACATCA GTATCCCACA GCCTCTCCAA GTCCCCCGGT 5340

CTCCCCCTCT TCTCGAAGGG ACCAAAAGAT CAATCCACCA CACCCGACGA CACTCAATTC 5400

CCCACCCCTA AAGGAGACAC CGGGAATCCC AGAATCAAGA CTCATCCAAT GTCCATCATG 5460

GGTCTCAAGG TGAACGTCTC TGCCATATTC ATGGCAGTAC TGTTAACTCT CCAAACACCC 5520

ACCGGTCAAA TCCATTGGGG CAATCTCTCT AAGATAGGGG TGGTAGGGAT AGGAAGTGCA 5580

AGCTACAAAG TTATGACTCG TTCCAGCCAT CAATCATTAG TCATAAAATT AATGCCCAAT 5640

ATAACTCTCC TCAATAACTG CACGAGGGTA GAGATTGCAG AATACAGGAG ACTACTGAGA 5700

ACAGTTTTGG AACCAATTAG AGATGCACTT AATGCAATGA CCCAGAATAT AAGACCGGTT 5760

CAGAGTGTAG CTTCAAGTAG GAGACACAAG AGATTTGCTG GAGTTGTCCT GGCGGGTGCG 5820

GCCCTAGGCG TTGCCACAGC TGCTCAGATA ACAGCCGGCA TTGCACTTCA CCAGTCCATG 5880

TTGAACTCTC AAGCCATCGA CAATCTGAGA GCGAGCCTGG AAACTACTAA TCAGGCAATT 5940

GAGGCAATCA GACAAGCAGG GCAGGAGATG ATATTGGCTG TTCAGGGTGT CCAAGACTAC 6000

ATCAATAATG AGCTGATACC GTCTATGAAC CAACTATCTT GTGATTTAAT CGGCCAGAAG 6060

CTAGGGCTCA AATTGCTCAG ATACTATACA GAAATCCTGT CACTATTTGG CCCCAGCTTA 6120

CGGGACCCCA TATCTGCGGA GATATCTATC CAGGCTTTGA GCTATGCGCT TGGAGGAGAT 6180

ATCAATAAGG TGTTAGAAAA GCTCGGATAC AGTGGAGGTG ATTTACTGGG CATCTTAGAG 6240

AGCAGAGGAA TAAAGGCCCG GATAACTCAC GTCGACACAG AGTCCTACTT CATTGTACTC 6300

AGTATAGCCT ATCCGACGCT GTCCGAGATT AAGGGGGTGA TTGTCCACCG GCTAGAAGGG 6360

GTCTCGTACA ACATAGGCTC TCAAGAGTGG TATACCACTG TGCCCAAGTA TGTTGCAACC 6420

CAAGGGTACC TTATCTCGAA TTTTGATGAG TCATCGTGTA CTTTCATGCC AGAGGGGACT 6480

GTGTGCAGCC AAAATGCCTT GTACCCGATG AGTCCTCTGC TCCAAGAATG CCTCCGGGGG 6540

TCCACCAAGT CCTGTGCTCG TACACTTGTA TCCGGGTCTT TTGGGAACCG GTTCATTTTA 6600

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AATCTGGGGA ATGCAATTGC TAAGTTGGAG GATGCCAAGG AATTGTTGGA GTCATCGGAC 6900

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TCTAGATGTA ACTAACTCAA TCGAGCATCA GGTCAAGGAC GTGCTGACAC CACTCTTCAA 7560

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TATATTAAAG AAAACTTTGA AAATACGAAG TTTCTATTCC CAGCTTTGTC TGGT 15894

(2) INFORMATION FOR SEQ ID NO:6:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2183 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

Met Asp Ser Leu Ser Val Asn Gln Ile Leu Tyr Pro Glu Val His Leu
1   5   10   15

Asp Ser Pro Ile Val Thr Asn Lys Ile Val Ala Ile Leu Glu Tyr Ala
            20   25   30

Arg Val Pro His Ala Tyr Ser Leu Glu Asp Pro Thr Leu Cys Gln Asn
        35   40   45

Ile Lys His Arg Leu Lys Asn Gly Phe Ser Asn Gln Met Ile Ile Asn
    50   55   60

Asn Val Glu Val Gly Asn Val Ile Lys Ser Lys Leu Arg Ser Tyr Pro
65   70   75   80

Thr His Ser His Ile Pro Tyr Pro Asn Cys Asn Gln Asp Leu Phe Asn
                85   90   95

Ile Glu Asp Lys Glu Ser Thr Arg Lys Ile Arg Glu Leu Leu Lys Lys
            100   105   110

Gly Asn Ser Leu Tyr Ser Lys Val Ser Asp Lys Val Phe Gln Cys Leu
        115   120   125

Arg Asp Thr Asn Ser Arg Leu Gly Leu Gly Ser Glu Leu Arg Glu Asp
    130   135   140

Ile Lys Glu Lys Ile Ile Asn Leu Gly Val Tyr Met His Ser Ser Gln
145   150   155   160

Trp Phe Glu Pro Phe Leu Phe Trp Phe Thr Val Lys Thr Glu Met Arg
                165   170   175

Ser Val Ile Lys Ser Gln Thr His Thr Cys His Arg Arg Arg His Thr
            180   185   190

Pro Val Phe Phe Thr Gly Ser Ser Val Glu Leu Leu Ile Ser Arg Asp
        195   200   205

Leu Val Ala Ile Ile Ser Lys Glu Ser Gln His Val Tyr Tyr Leu Thr
    210   215   220

Phe Glu Leu Val Leu Met Tyr Cys Asp Val Ile Glu Gly Arg Leu Met
225   230   235   240

Thr Glu Thr Ala Met Thr Ile Asp Ala Arg Tyr Thr Glu Leu Leu Gly
                245   250   255

Arg Val Arg Tyr Met Trp Lys Leu Ile Asp Gly Phe Phe Pro Ala Leu
            260   265   270

Gly Asn Pro Thr Tyr Gln Ile Val Ala Met Leu Glu Pro Leu Ser Leu

275 280 285

Ala Tyr Leu Gln Leu Arg Asp Ile Thr Val Glu Leu Arg Gly Ala Phe
290 295 300

Leu Asn His Cys Phe Thr Glu Ile His Asp Val Leu Asp Gln Asn Gly
305 310 315 320

Phe Ser Asp Glu Gly Thr Tyr His Glu Leu Ile Glu Ala Leu Asp Tyr
325 330 335

Ile Phe Ile Thr Asp Asp Ile His Leu Thr Gly Glu Ile Phe Ser Phe
340 345 350

Phe Arg Ser Phe Gly His Pro Arg Leu Glu Ala Val Thr Ala Ala Glu
355 360 365

Asn Val Arg Lys Tyr Met Asn Gln Pro Lys Val Ile Val Tyr Glu Thr
370 375 380

Leu Met Lys Gly His Ala Ile Phe Cys Gly Ile Ile Ile Asn Gly Tyr
385 390 395 400

Arg Asp Arg His Gly Gly Ser Trp Pro Pro Leu Thr Leu Pro Leu His
405 410 415

Ala Ala Asp Thr Ile Arg Asn Ala Gln Ala Ser Gly Glu Gly Leu Thr
420 425 430

His Glu Gln Cys Val Asp Asn Trp Lys Ser Phe Ala Gly Val Lys Phe
435 440 445

Gly Cys Phe Met Pro Leu Ser Leu Asp Ser Asp Leu Thr Met Tyr Leu
450 455 460

Lys Asp Lys Ala Leu Ala Ala Leu Gln Arg Glu Trp Asp Ser Val Tyr
465 470 475 480

Pro Lys Glu Phe Leu Arg Tyr Asp Pro Pro Lys Gly Thr Gly Ser Arg
485 490 495

Arg Leu Val Asn Val Phe Leu Asn Asp Ser Ser Phe Asp Pro Tyr Asp
500 505 510

Met Ile Met Tyr Val Val Ser Gly Ala Tyr Leu His Asp Pro Glu Phe
515 520 525

Asn Leu Ser Tyr Ser Leu Lys Glu Lys Glu Ile Lys Glu Thr Gly Arg
530 535 540

Leu Phe Ala Lys Met Thr Tyr Lys Met Arg Ala Cys Gln Val Ile Ala
545 550 555 560

Glu Asn Leu Ile Ser Asn Gly Ile Gly Asn Tyr Phe Lys Asp Asn Gly
565 570 575

Met Ala Lys Asp Glu His Asp Leu Thr Lys Ala Leu His Thr Leu Ala
580 585 590

Val Ser Gly Val Pro Lys Asp Leu Lys Glu Ser His Arg Gly Gly Pro
595 600 605

Val Leu Lys Thr His Ser Arg Ser Pro Val His Thr Ser Thr Lys Asn
610 615 620

Val Arg Ala Ala Lys Gly Phe Ile Gly Phe Pro His Val Ile Arg Gln
625 630 635 640

Asp Gln Asp Thr Asp His Pro Glu Asn Met Glu Ala Tyr Glu Thr Val
645 650 655

Ser Ala Phe Ile Thr Thr Asp Leu Lys Lys Tyr Cys Leu Asn Trp Arg
660 665 670

Tyr Glu Thr Ile Ser Leu Phe Ala Gln Arg Leu Asn Glu Ile Tyr Gly
675 680 685

Leu Pro Ser Phe Phe Gln Trp Leu His Lys Arg Leu Glu Thr Ser Val
690 695 700

Leu Tyr Val Ser Asp Pro His Cys Pro Pro Asp Leu Asp Ala His Val
705 710 715 720

Pro Leu Cys Lys Val Pro Asn Asp Gln Ile Phe Ile Lys Tyr Pro Met
725 730 735

Gly Gly Ile Glu Gly Tyr Cys Gln Lys Leu Trp Thr Ile Ser Thr Ile
740 745 750

Pro Tyr Leu Tyr Leu Ala Ala Tyr Glu Ser Gly Val Arg Ile Ala Ser
755 760 765

Leu Val Gln Gly Asp Asn Gln Thr Ile Ala Val Thr Lys Arg Val Pro
770 775 780

Ser Thr Trp Pro Tyr Asn Leu Lys Lys Arg Glu Ala Ala Arg Val Thr
785 790 795 800

Arg Asp Tyr Phe Val Ile Leu Arg Gln Arg Leu His Asp Ile Gly His
805 810 815

His Leu Lys Ala Asn Glu Thr Ile Val Ser Ser His Phe Phe Val Tyr
820 825 830

Ser Lys Gly Ile Tyr Tyr Asp Gly Leu Leu Val Ser Gln Ser Leu Lys
835 840 845

Ser Ile Ala Arg Cys Val Phe Trp Ser Glu Thr Ile Val Asp Glu Thr
850 855 860

Arg Ala Ala Cys Ser Asn Ile Ala Thr Thr Met Ala Lys Ser Ile Glu
865 870 875 880

Arg Gly Tyr Asp Arg Tyr Leu Ala Tyr Ser Leu Asn Val Leu Lys Val
885 890 895

Ile Gln Gln Ile Leu Ile Ser Leu Gly Phe Thr Ile Asn Ser Thr Met
900 905 910

Thr Arg Asp Val Val Ile Pro Leu Leu Thr Asn Asn Asp Leu Leu Ile
915 920 925

Arg Met Ala Leu Leu Pro Ala Pro Ile Gly Gly Met Asn Tyr Leu Asn
930 935 940

Met Ser Arg Leu Phe Val Arg Asn Ile Gly Asp Pro Val Thr Ser Ser
945 950 955 960

Ile Ala Asp Leu Lys Arg Met Ile Leu Ser Ser Leu Met Pro Glu Glu
965 970 975

Thr Leu His Gln Val Met Thr Gln Gln Pro Gly Asp Ser Ser Phe Leu
980 985 990

Asp Trp Ala Ser Asp Pro Tyr Ser Ala Asn Leu Val Cys Val Gln Ser
995 1000 1005

Ile Thr Arg Leu Leu Lys Asn Ile Thr Ala Arg Phe Val Leu Ile His
1010 1015 1020

Ser Pro Asn Pro Met Leu Lys Gly Leu Phe His Asp Asp Ser Lys Glu
1025 1030 1035 1040

Glu Asp Glu Gly Leu Ala Ala Phe Leu Met Asp Arg His Ile Ile Val
1045 1050 1055

Pro Arg Ala Ala His Glu Ile Leu Asp His Ser Val Thr Gly Ala Arg
1060 1065 1070

Glu Ser Ile Ala Gly Met Leu Asp Thr Thr Lys Gly Leu Ile Arg Ala
1075 1080 1085

Ser Met Arg Lys Gly Gly Leu Thr Ser Arg Val Ile Thr Arg Leu Ser
1090 1095 1100

Asn Tyr Asp Tyr Glu Gln Phe Arg Ala Gly Met Val Leu Leu Thr Gly

1105 1110 1115 1120

Arg Lys Arg Asn Val Leu Ile Asp Lys Glu Ser Cys Ser Val Gln Leu
1125 1130 1135

Ala Arg Ala Leu Arg Ser His Met Trp Ala Arg Leu Ala Arg Gly Arg
1140 1145 1150

Pro Ile Tyr Gly Leu Glu Val Pro Asp Val Leu Glu Ser Met Arg Gly
1155 1160 1165

His Leu Ile Arg Arg His Glu Thr Cys Val Ile Cys Glu Cys Gly Ser
1170 1175 1180

Val Asn Tyr Gly Trp Phe Phe Val Pro Ser Gly Cys Gln Leu Asp Asp
1185 1190 1195 1200

Ile Asp Lys Glu Thr Ser Ser Leu Arg Val Pro Tyr Ile Gly Ser Thr
1205 1210 1215

Thr Asp Glu Arg Thr Asp Met Lys Leu Ala Phe Val Arg Ala Pro Ser
1220 1225 1230

Arg Ser Leu Arg Ser Ala Val Arg Ile Ala Thr Val Tyr Ser Trp Ala
1235 1240 1245

Tyr Gly Asp Asp Asp Ser Ser Trp Asn Glu Ala Trp Leu Leu Ala Arg
1250 1255 1260

Gln Arg Ala Asn Val Ser Leu Glu Glu Leu Arg Val Ile Thr Pro Ile
1265 1270 1275 1280

Ser Thr Ser Thr Asn Leu Ala His Arg Leu Arg Asp Arg Thr Thr Gln
1285 1290 1295

Val Lys Tyr Ser Gly Thr Ser Leu Val Arg Val Ala Arg Tyr Thr Thr
1300 1305 1310

Ile Ser Asn Asp Asn Leu Ser Phe Val Ile Ser Asp Lys Lys Val Asp
1315 1320 1325

Thr Asn Phe Ile Tyr Gln Gln Gly Met Leu Leu Gly Leu Gly Val Leu
1330 1335 1340

Glu Thr Leu Phe Arg Leu Glu Lys Asp Thr Gly Ser Ser Asn Thr Val
1345 1350 1355 1360

Leu His Leu His Val Glu Thr Asp Cys Cys Val Ile Pro Met Ile Asp
1365 1370 1375

His Pro Arg Ile Pro Ser Ser Arg Lys Leu Glu Leu Arg Ala Glu Leu
1380 1385 1390

Cys Thr Asn Pro Leu Ile Tyr Asp Asn Ala Pro Leu Ile Asp Arg Asp
1395 1400 1405

Ala Thr Arg Leu Tyr Thr Gln Ser His Arg Arg His Leu Val Glu Phe
1410 1415 1420

Val Thr Trp Ser Thr Pro Gln Leu Tyr His Ile Leu Ala Lys Ser Thr
1425 1430 1435 1440

Ala Leu Ser Met Ile Asp Leu Val Thr Lys Phe Glu Lys Asp His Met
1445 1450 1455

Asn Glu Ile Ser Ala Leu Ile Gly Asp Asp Asp Ile Asn Ser Phe Ile
1460 1465 1470

Thr Glu Phe Leu Leu Ile Glu Pro Arg Leu Phe Thr Ile Tyr Leu Gly
1475 1480 1485

Gln Cys Ala Ala Ile Asn Trp Ala Phe Asp Val His Tyr His Arg Pro
1490 1495 1500

Ser Gly Lys Tyr Gln Met Gly Glu Leu Leu Ser Ser Phe Leu Ser Arg
1505 1510 1515 1520

Met Ser Lys Gly Val Phe Lys Val Leu Val Asn Ala Leu Ser His Pro
1525 1530 1535

Lys Ile Tyr Lys Lys Phe Trp His Cys Gly Ile Ile Glu Pro Ile His
1540 1545 1550

Gly Pro Ser Leu Asp Ala Gln Asn Leu His Thr Thr Val Cys Asn Met
1555 1560 1565

Ile Tyr Thr Cys Tyr Met Thr Tyr Leu Asp Leu Leu Leu Asn Glu Glu
1570 1575 1580

Leu Glu Glu Phe Thr Phe Leu Leu Cys Glu Ser Asp Glu Asp Val Val
1585 1590 1595 1600

Pro Asp Arg Phe Asp Asn Ile Gln Ala Lys His Leu Cys Val Leu Ala
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Asp Leu Tyr Cys Gln Pro Gly Thr Cys Pro Pro Ile Arg Gly Leu Arg
1620 1625 1630

Pro Val Glu Lys Cys Ala Val Leu Thr Asp His Ile Lys Ala Glu Ala
1635 1640 1645

Arg Leu Ser Pro Ala Gly Ser Ser Trp Asn Ile Asn Pro Ile Ile Val
1650 1655 1660

Asp His Tyr Ser Cys Ser Leu Thr Tyr Leu Arg Arg Gly Ser Ile Lys
1665 1670 1675 1680

Gln Ile Arg Leu Arg Val Asp Pro Gly Phe Ile Phe Asp Ala Leu Ala
1685 1690 1695

Glu Val Asn Val Ser Gln Pro Lys Ile Gly Ser Asn Asn Ile Ser Asn
1700 1705 1710

Met Ser Ile Lys Asp Phe Arg Pro Pro His Asp Asp Val Ala Lys Leu
1715 1720 1725

Leu Lys Asp Ile Asn Thr Ser Lys His Asn Leu Pro Ile Ser Gly Gly
1730 1735 1740

Asn Leu Ala Asn Tyr Glu Ile His Ala Phe Arg Arg Ile Gly Leu Asn
1745 1750 1755 1760

Ser Ser Ala Cys Tyr Lys Ala Val Glu Ile Ser Thr Leu Ile Arg Arg
1765 1770 1775

Cys Leu Glu Pro Gly Glu Asp Gly Leu Phe Leu Gly Glu Gly Ser Gly
1780 1785 1790

Ser Met Leu Ile Thr Tyr Lys Glu Ile Leu Lys Leu Asn Lys Cys Phe
1795 1800 1805

Tyr Asn Ser Gly Val Ser Ala Asn Ser Arg Ser Gly Gln Arg Glu Leu
1810 1815 1820

Ala Pro Tyr Pro Ser Glu Val Gly Leu Val Glu His Arg Met Gly Val
1825 1830 1835 1840

Gly Asn Ile Val Lys Val Leu Phe Asn Gly Arg Pro Glu Val Thr Trp
1845 1850 1855

Val Gly Ser Val Asp Cys Phe Asn Phe Ile Val Ser Asn Ile Pro Thr
1860 1865 1870

Ser Ser Val Gly Phe Ile His Ser Asp Ile Glu Thr Leu Pro Asn Lys
1875 1880 1885

Asp Thr Ile Glu Lys Leu Glu Glu Leu Ala Ala Ile Leu Ser Met Ala
1890 1895 1900

Leu Leu Leu Gly Lys Ile Gly Ser Ile Leu Val Ile Lys Leu Met Pro
1905 1910 1915 1920

Phe Ser Gly Asp Phe Val Gln Gly Phe Ile Ser Tyr Val Gly Ser Tyr
1925 1930 1935

Tyr Arg Glu Val Asn Leu Val Tyr Pro Arg Tyr Ser Asn Phe Ile Ser

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            1940                1945                1950

Thr Glu Ser Tyr Leu Val Met Thr Asp Leu Lys Ala Asn Arg Leu Met
        1955                1960                1965

Asn Pro Glu Lys Ile Lys Gln Gln Ile Ile Glu Ser Ser Val Arg Thr
    1970                1975                1980

Ser Pro Gly Leu Ile Gly His Ile Leu Ser Ile Lys Gln Leu Ser Cys
1985                1990                1995                2000

Ile Gln Ala Ile Val Gly Asp Ala Val Ser Arg Gly Gly Ile Asn Pro
                2005                2010                2015

Ile Leu Lys Lys Leu Thr Pro Ile Glu Gln Val Leu Ile Asn Cys Gly
            2020                2025                2030

Leu Ala Ile Asn Gly Pro Lys Leu Cys Lys Glu Leu Ile His His Asp
        2035                2040                2045

Val Ala Ser Gly Gln Asp Gly Leu Leu Asn Ser Ile Leu Ile Leu Tyr
    2050                2055                2060

Arg Glu Leu Ala Arg Phe Lys Asp Asn Gln Arg Ser Gln Gln Gly Met
2065                2070                2075                2080

Phe His Ala Tyr Pro Val Leu Val Ser Ser Arg Gln Arg Glu Leu Ile
                2085                2090                2095

Ser Arg Ile Thr Arg Lys Phe Trp Gly His Ile Leu Leu Tyr Ser Gly
            2100                2105                2110

Asn Arg Lys Leu Ile Asn Arg Phe Ile Gln Asn Leu Lys Ser Gly Tyr
        2115                2120                2125

Leu Ile Leu Asp Leu His Gln Asn Ile Phe Val Lys Asn Leu Ser Lys
    2130                2135                2140

Ser Glu Lys Gln Ile Ile Met Thr Gly Gly Leu Lys Arg Glu Trp Val
2145                2150                2155                2160

Phe Lys Val Thr Ile Lys Glu Thr Lys Glu Trp Tyr Lys Leu Val Gly
                2165                2170                2175

Tyr Ser Ala Leu Ile Lys Asp
            2180
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(2) INFORMATION FOR SEQ ID NO:7:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 15894 base pairs
(B) TYPE: nucleic acid

(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

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TGAGGAGCTT AGCATTGTTC AAAAGAAACA AGGACAAACC ACCCATTACA TCAGGATCCG 180

GTGGAGCCAT CAGAGGAATC AAACACATTA TTATAGTACC AATTCCTGGA GATTCCTCAA 240

TTACCACTCG ATCCAGACTA CTGGACCGGT TGGTCAGGTT AATTGGAAAC CCGGATGTGA 300

GCGGGCCCAA ACTAACAGGG GCACTAATAG GTATATTATC CTTATTTGTG GAGTCTCCAG 360

GTCAATTGAT TCAGAGGATC ACCGATGACC CTGACGTTAG CATCAGGCTG TTAGAGGTTG 420

TTCAGAGTGA CCAGTCACAA TCTGGCCTTA CCTTCGCATC AAGAGGTACC AACATGGAGG 480

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CAGACACGGC AGCTGATTCG GAGCTAAGAA GGTGGATAAA GTACACCCAA CAAAGAAGGG 720

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GATTAGCCAG TTTTATCTTG ACTATTAAGT TTGGGATAGA AACTATGTAT CCTGCTCTTG 960

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TGAACATGAG CAGGCTGTTT GTCAGAAACA TCGGTGATCC AGTAACATCA TCAATTGCTG 12120

ATCTCAAGAG AATGATTCTC GCATCACTAA TGCCTGAAGA GACCCTCCAT CAAGTAATGA 12180

CACAACAACC GGGGGACTCT TCATTCCTAG ACTGGGCTAG CGACCCTTAC TCAGCAAATC 12240

TTGTATGCGT CCAGAGCATC ACTAGACTCC TCAAGAACAT AACTGCAAGG TTTGTCCTAA 12300

TCCATAGTCC AAACCCAATG TTAAAAGGGT TATTCCATGA TGACAGTAAA GAAGAGGACG 12360

AGAGACTGGC GGCATTCCTC ATGGACAGGC ATATTATAGT ACCTAGGGCA GCTCATGAAA 12420

TCCTGGATCA TAGTGTCACA GGGGCAAGAG AGTCTATTGC AGGCATGCTA GATACCACAA 12480

AAGGCCTGAT TCGAGCCAGC ATGAGGAAGG GGGGGTTAAC CTCTCGAGTG ATAACCAGAT 12540

TGTCCAATTA TGACTATGAA CAATTTAGAG CAGGGATGGT GCTATTGACA GGAAGAAAGA 12600

GAAATGTCCT CATTGACAAA GAGTCATGTT CAGTGCAGCT GGCTAGAGCC CTAAGAAGCC 12660

ATATGTGGGC AAGACTAGCT CGAGGACGGC CTATTTACGG CCTTGAGGTC CCTGATGTAC 12720

TAGAATCTAT GCGAGGCCAC CTTATTCGGC GTCATGAGAC ATGTGTCATC TGCGAGTGTG 12780

GATCAGTCAA CTACGGATGG TTTTTTGTCC CCTCGGGTTG CCAACTGGAT GATATTGACA 12840

AGGAAACATC ATCCTTGAGA GTCCCATATA TTGGTTCTAC CACTGATGAG AGAACAGACA 12900

TGAAGCTTGC CTTCGTAAGA GCCCCAAGTA GATCCTTGCG ATCTGCCGTT AGAATAGCAA 12960

CAGTGTACTC ATGGGCTTAC GGTGATGATG ATAGCTCTTG GAACGAAGCC TGGTTGTTGG 13020

CAAGGCAAAG GGCCAATGTG AGCCTGGAGG AGCTAAGGGT GATCACTCCC ATCTCGACTT 13080

CGACTAATTT AGCGCATAGG TTGAGGGATC GTAGCACTCA AGTGAAATAC TCAGGTACAT 13140

CCCTTGTCAG AGTGGCAAGG TATACCACAA TCTCCAACGA CAATCTCTCA TTTGTCATAT 13200

CAGATAAGAA AGTTGATACT AACTTTATAT ACCAACAAGG AATGCTTCTA GGGTTGGGTG 13260

TTTTAGAAAC ATTGTTTCGA CTCGAGAAAG ATACTGGATC ATCTAACACG GTATTACATC 13320

TTCACGTCGA AACAGATTGT TGCGTGATCC CGATGATAGA TCATCCCAGG ATACCCAGCT 13380

CCCGCAAGCT AGAGCTGAGG GCAGAGCTAT GTACCAACCC ATTGATATAT GATAATGCAC 13440

CTTTAATTGA CAGAGATGCA ACAAGGCTAT ACACCCAGAG CCATAGGAGG CACCTTGTGG 13500

AATTTGTTAC ATGGTCCACA CCCCAACTAT ATCACATTCT AGCTAAGTCC ACAGCACTAT 13560

CTATGATTGA CCTGGTAACA AAATTTGAGA AGGACCATAT GAATGAAATT TCAGCTCTCA 13620

TAGGGGATGA CGATATCAAT AGTTTCATAA CTGAGTTTCT GCTTATAGAG CCAAGATTAT 13680

TCACCATCTA CTTGGGCCAG TGTGCAGCCA TCAATTGGGC ATTTGATGTA CATTATCATA 13740

GACCATCAGG GAAATATCAG ATGGGTGAGC TGTTGTCTTC GTTCCTTTCT AGAATGAGCA 13800

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GGCATTGTGG TATTATAGAG CCTATCCATG GTCCTTCACT TGATGCTCAA AACTTGCACA 13920

CAACTGTGTG CAACATGGTT TACACATGCT ATATGACCTA CCTTGACCTG TTGTTGAATG 13980

AAGAGTTAGA AGAGTTCACA TTTCTTTTGT GTGAAAGCGA TGAGGATGTA GTACCGGACA 14040

GATTCGACAA CATCCAGGCA AAACACTTGT GTGTTCTGGC AGATTTGTAC TGTCAACCAG 14100

GGACCTGCCC ACCGATTCGA GGTCTAAGGC CGGTAGAGAA ATGTGCAGTT CTAACCGATC 14160

ATATCAAGGC AGAGGCTAGG TTATCTCCAG CAGGATCTTC GTGGAACATA AATCCAATTA 14220

TTGTAGACCA TTACTCATGC TCTCTGACTT ATCTCCGTCG AGGATCTATC AAACAGATAA 14280

GATTGAGAGT TGATCCAGGA TTCATTTTTG ATGCCCTCGC TGAGGTAAAT GTCAGTCAGC 14340

CAAAGGTCGG CAGCAACAAC ATCTCAAATA TGAGCATCAA GGATTTCAGA CCTCCACACG 14400

ATGATGTTGC AAAATTGCTC AAAGATATCA ACACAAGCAA GCACAATCTT CCCATTTCAG 14460

GGGGTAGTCT TGCCAATTAT GAAATCCATG CTTTCCGCAG AATCGGGTTA AACTCATCTG 14520

CTTGCTACAA AGCTGTTGAG ATATCAACAT TAATTAGGAG ATGCCTTGAG CCAGGGGAAG 14580

ACGGCTTGTT CTTGGGTGAG GGGTCGGGTT CTATGTTGAT CACTTATAAG GAGATACTAA 14640

AACTAAACAA GTGCTTCTAT AATAGTGGGG TTTCCGCCAA TTCTAGATCT GGTCAAAGGG 14700

AATTAGCACC CTATCCCTCC GAAGTTGGCC TTGTCGAACA CAGAATGGGA GTAGGTAATA 14760

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TCAATTTCAT AGTCAGTAAT ATCCCTACCT CTAGTGTGGG ATTTATCCAT TCAGATATAG 14880

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TGGCTCTACT CCTTGGCAAA ATAGGATCAA TACTGGTGAT TAAGCTTATG CCTTTCAGCG 15000

GGGATTTTGT TCAGGGATTT ATAAGCTATG TAGGGTCTCA TTATAGAGAA GTGAACCTTG 15060

TCTACCCTAG GTACAGCAAC TTCATATCTA CTGAATCTTA TTTAGTTATG ACAGATCTCA 15120

AAGCTAACCG GCTAATGAAT CCTGAAAAGA TTAAGCAGCA GATAATTGAA TCATCTGTGC 15180

GGACTTCACC TGGACTTATA GGTCACATCC TATCTATCAA GCAACTAAGC TGCATACAAG 15240

CAATTGTGGG AGGCGCAGTT AGTAGAGGTG ATATCAACCC TATTCTGAAA AAACTTACAC 15300

CTATAGAGCA GGTGCTGATC AGTTGCGGGT TGGCAATTAA CGGACCTAAG CTGTGCAAAG 15360

AATTAATCCA CCATGATGTT GCCTCAGGGC AAGATGGATT GCTTAACTCT ATACTCATCC 15420

TCTACAGGGA GTTGGCAAGA TTCAAAGACA ACCAAAGAAG TCAACAAGGG ATGTTCCACG 15480

CTTACCCCGT ATTGGTAAGT AGTAGGCAAC GAGAACTTGT ATCTAGGATC ACTCGCAAAT 15540

TTTGGGGGCA TATTCTTCTT TACTCCGGGA ACAGAAAGTT GATAAATCGG TTTATCCAGA 15600

ATCTCAAGTC CGGTTATCTA ATACTAGACT TACACCAGAA TATCTTCGTT AAGAATCTAT 15660

CCAAGTCAGA GAAACAGATT ATTATGACGG GGGGTTTAAA ACGTGAGTGG GTTTTTAAGG 15720

TAACAGTCAA GGAGACCAAA GAATGGTATA AGTTAGTCGG ATACAGCGCT CTGATTAAGG 15780

ATTAATTGGT TGAACTCCGG AACCCTAATC CTACCCTAGG TAGTTAGGCA TTATTTGCAA 15840

TATATTAAAG AAAACTTTGA AAATACGAAG TTTCTATTCC CAGCTTTGTC TGGT 15894

(2) INFORMATION FOR SEQ ID NO:8:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2183 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

Met Asp Ser Leu Ser Val Asn Gln Ile Leu Tyr Pro Glu Val His Leu
1 5 10 15

Asp Ser Pro Ile Val Thr Asn Lys Ile Val Ala Ile Leu Glu Tyr Ala
20 25 30

Arg Val Pro His Ala Tyr Ser Leu Glu Asp Pro Thr Leu Cys Gln Asn
35 40 45

Ile Lys His Arg Leu Lys Asn Gly Phe Ser Asn Gln Met Ile Ile Asn
50 55 60

Asn Val Glu Val Gly Asn Val Ile Lys Ser Lys Leu Arg Ser Tyr Pro
65 70 75 80

Ala His Ser His Ile Pro Tyr Pro Asn Cys Asn Gln Asp Leu Phe Asn
85 90 95

Ile Glu Asp Lys Glu Ser Thr Arg Lys Ile Arg Glu Leu Leu Lys Lys
100 105 110

Gly Asn Ser Leu Tyr Ser Lys Val Ser Asp Lys Val Phe Gln Cys Leu
115 120 125

Arg Asp Thr Asn Ser Arg Leu Gly Leu Gly Ser Glu Leu Arg Glu Asp
130 135 140

Ile Lys Glu Lys Ile Ile Asn Leu Gly Val Tyr Met His Ser Ser Gln
145 150 155 160

Trp Phe Glu Pro Phe Leu Phe Trp Phe Thr Val Lys Thr Glu Met Arg
165 170 175

Ser Val Ile Lys Ser Gln Thr His Thr Cys His Arg Arg Arg His Thr
180 185 190

Pro Val Phe Phe Thr Gly Ser Ser Val Glu Leu Leu Ile Ser Arg Asp
195 200 205

Leu Val Ala Ile Ile Ser Lys Glu Ser Gln His Val Tyr Tyr Leu Thr
210 215 220

Phe Glu Leu Val Leu Met Tyr Cys Asp Val Ile Glu Gly Arg Leu Met
225 230 235 240

Thr Glu Thr Ala Met Thr Ile Asp Ala Arg Tyr Ala Glu Leu Leu Gly
245 250 255

Arg Val Arg Tyr Met Trp Lys Leu Ile Asp Gly Phe Phe Pro Ala Leu
260 265 270

Gly Asn Pro Thr Tyr Gln Ile Val Ala Met Leu Glu Pro Leu Ser Leu
275 280 285

Ala Tyr Leu Gln Leu Arg Asp Ile Thr Val Glu Leu Arg Gly Ala Phe
290 295 300

Leu Asn His Cys Phe Thr Glu Ile His Asp Val Leu Asp Gln Asn Gly
305 310 315 320

Phe Ser Asp Glu Gly Thr Tyr His Glu Leu Ile Glu Ala Leu Asp Tyr
325 330 335

Ile Phe Ile Thr Asp Asp Ile His Leu Thr Gly Glu Ile Phe Ser Phe
340 345 350

Phe Arg Ser Phe Gly His Pro Arg Leu Glu Ala Val Thr Ala Ala Glu
355 360 365

Asn Val Arg Lys Tyr Met Asn Gln Pro Lys Val Ile Val Tyr Glu Thr
370 375 380

Leu Met Lys Gly His Ala Ile Phe Cys Gly Ile Ile Ile Asn Gly Tyr
385 390 395 400

Arg Asp Arg His Gly Gly Ser Trp Pro Pro Leu Thr Leu Pro Leu His
405 410 415

Ala Ala Asp Thr Ile Arg Asn Ala Gln Ala Ser Gly Glu Gly Leu Thr
420 425 430

His Glu Gln Cys Val Asp Asn Trp Arg Ser Phe Ala Gly Val Arg Phe
435 440 445

Gly Cys Phe Met Pro Leu Ser Leu Asp Ser Asp Leu Thr Met Tyr Leu
450 455 460

Lys Asp Lys Ala Leu Ala Ala Leu Gln Arg Glu Trp Asp Ser Val Tyr
465 470 475 480

Pro Lys Glu Phe Leu Arg Tyr Asp Pro Pro Lys Gly Thr Gly Ser Arg
485 490 495

Arg Leu Val Asp Val Phe Leu Asn Asp Ser Ser Phe Asp Pro Tyr Asp
500 505 510

Met Ile Met Tyr Val Val Ser Gly Ala Tyr Leu His Asp Pro Glu Phe
515 520 525

Asn Leu Ser Tyr Ser Leu Lys Glu Lys Glu Ile Lys Glu Thr Gly Arg
530 535 540

Leu Phe Ala Lys Met Thr Tyr Lys Met Arg Ala Cys Gln Val Ile Ala
545 550 555 560

Glu Asn Leu Ile Ser Asn Gly Ile Gly Lys Tyr Phe Lys Asp Asn Gly
565 570 575

Met Ala Lys Asp Glu His Asp Leu Thr Lys Ala Leu His Thr Leu Ala
580 585 590

Val Ser Gly Val Pro Lys Asp Leu Lys Glu Ser His Arg Gly Gly Pro
595 600 605

Val Leu Lys Thr Tyr Ser Arg Ser Pro Val His Thr Ser Thr Arg Asn
610 615 620

Val Lys Ala Glu Lys Gly Phe Val Gly Phe Pro His Val Ile Arg Gln
625 630 635 640

Asn Gln Asp Thr Asp His Pro Glu Asn Ile Glu Thr Tyr Glu Thr Val

645 650 655

Ser Ala Phe Ile Thr Thr Asp Leu Lys Lys Tyr Cys Leu Asn Trp Arg
660 665 670

Tyr Glu Thr Ile Ser Leu Phe Ala Gln Arg Leu Asn Glu Ile Tyr Gly
675 680 685

Leu Pro Ser Phe Phe Gln Trp Leu His Lys Arg Leu Glu Thr Ser Val
690 695 700

Leu Tyr Val Ser Asp Pro His Cys Pro Pro Asp Leu Asp Ala His Val
705 710 715 720

Pro Leu Cys Lys Val Pro Asn Asp Gln Ile Phe Ile Lys Tyr Pro Met
725 730 735

Gly Gly Ile Glu Gly Tyr Cys Gln Lys Leu Trp Thr Ile Ser Thr Ile
740 745 750

Pro Tyr Leu Tyr Leu Ala Ala Tyr Glu Ser Gly Val Arg Ile Ala Ser
755 760 765

Leu Val Gln Gly Asp Asn Gln Thr Ile Ala Val Thr Lys Arg Val Pro
770 775 780

Ser Thr Trp Pro Tyr Asn Leu Lys Lys Arg Glu Ala Ala Arg Val Thr
785 790 795 800

Arg Asp Tyr Phe Val Ile Leu Arg Gln Arg Leu His Asp Ile Gly His
805 810 815

His Leu Lys Ala Asn Glu Thr Ile Val Ser Ser His Phe Phe Val Tyr
820 825 830

Ser Lys Gly Ile Tyr Tyr Asp Gly Leu Leu Val Ser Gln Ser Leu Lys
835 840 845

Ser Ile Ala Arg Cys Val Phe Trp Ser Glu Thr Ile Val Asp Glu Thr
850 855 860

Arg Ala Ala Cys Ser Asn Ile Ala Thr Thr Met Ala Lys Ser Ile Glu
865 870 875 880

Arg Gly Tyr Asp Arg Tyr Leu Ala Tyr Ser Leu Asn Val Leu Lys Val
885 890 895

Ile Gln Gln Ile Leu Ile Ser Leu Gly Phe Thr Ile Asn Ser Thr Met
900 905 910

Thr Arg Asp Val Val Ile Pro Leu Leu Thr Asn Asn Asp Leu Leu Ile
915 920 925

Arg Met Ala Leu Leu Pro Ala Pro Ile Gly Gly Met Asn Tyr Leu Asn
930 935 940

Met Ser Arg Leu Phe Val Arg Asn Ile Gly Asp Pro Val Thr Ser Ser
945 950 955 960

Ile Ala Asp Leu Lys Arg Met Ile Leu Ala Ser Leu Met Pro Glu Glu
965 970 975

Thr Leu His Gln Val Met Thr Gln Gln Pro Gly Asp Ser Ser Phe Leu
980 985 990

Asp Trp Ala Ser Asp Pro Tyr Ser Ala Asn Leu Val Cys Val Gln Ser
995 1000 1005

Ile Thr Arg Leu Leu Lys Asn Ile Thr Ala Arg Phe Val Leu Ile His
1010 1015 1020

Ser Pro Asn Pro Met Leu Lys Gly Leu Phe His Asp Asp Ser Lys Glu
1025 1030 1035 1040

Glu Asp Glu Arg Leu Ala Ala Phe Leu Met Asp Arg His Ile Ile Val
1045 1050 1055

Pro Arg Ala Ala His Glu Ile Leu Asp His Ser Val Thr Gly Ala Arg
1060 1065 1070

Glu Ser Ile Ala Gly Met Leu Asp Thr Thr Lys Gly Leu Ile Arg Ala
1075 1080 1085

Ser Met Arg Lys Gly Gly Leu Thr Ser Arg Val Ile Thr Arg Leu Ser
1090 1095 1100

Asn Tyr Asp Tyr Glu Gln Phe Arg Ala Gly Met Val Leu Leu Thr Gly
1105 1110 1115 1120

Arg Lys Arg Asn Val Leu Ile Asp Lys Glu Ser Cys Ser Val Gln Leu
1125 1130 1135

Ala Arg Ala Leu Arg Ser His Met Trp Ala Arg Leu Ala Arg Gly Arg
1140 1145 1150

Pro Ile Tyr Gly Leu Glu Val Pro Asp Val Leu Glu Ser Met Arg Gly
1155 1160 1165

His Leu Ile Arg Arg His Glu Thr Cys Val Ile Cys Glu Cys Gly Ser
1170 1175 1180

Val Asn Tyr Gly Trp Phe Phe Val Pro Ser Gly Cys Gln Leu Asp Asp
1185 1190 1195 1200

Ile Asp Lys Glu Thr Ser Ser Leu Arg Val Pro Tyr Ile Gly Ser Thr
1205 1210 1215

Thr Asp Glu Arg Thr Asp Met Lys Leu Ala Phe Val Arg Ala Pro Ser
1220 1225 1230

Arg Ser Leu Arg Ser Ala Val Arg Ile Ala Thr Val Tyr Ser Trp Ala
1235 1240 1245

Tyr Gly Asp Asp Asp Ser Ser Trp Asn Glu Ala Trp Leu Leu Ala Arg
1250 1255 1260

Gln Arg Ala Asn Val Ser Leu Glu Glu Leu Arg Val Ile Thr Pro Ile
1265 1270 1275 1280

Ser Thr Ser Thr Asn Leu Ala His Arg Leu Arg Asp Arg Ser Thr Gln
1285 1290 1295

Val Lys Tyr Ser Gly Thr Ser Leu Val Arg Val Ala Arg Tyr Thr Thr
1300 1305 1310

Ile Ser Asn Asp Asn Leu Ser Phe Val Ile Ser Asp Lys Lys Val Asp
1315 1320 1325

Thr Asn Phe Ile Tyr Gln Gln Gly Met Leu Leu Gly Leu Gly Val Leu
1330 1335 1340

Glu Thr Leu Phe Arg Leu Glu Lys Asp Thr Gly Ser Ser Asn Thr Val
1345 1350 1355 1360

Leu His Leu His Val Glu Thr Asp Cys Cys Val Ile Pro Met Ile Asp
1365 1370 1375

His Pro Arg Ile Pro Ser Ser Arg Lys Leu Glu Leu Arg Ala Glu Leu
1380 1385 1390

Cys Thr Asn Pro Leu Ile Tyr Asp Asn Ala Pro Leu Ile Asp Arg Asp
1395 1400 1405

Ala Thr Arg Leu Tyr Thr Gln Ser His Arg Arg His Leu Val Glu Phe
1410 1415 1420

Val Thr Trp Ser Thr Pro Gln Leu Tyr His Ile Leu Ala Lys Ser Thr
1425 1430 1435 1440

Ala Leu Ser Met Ile Asp Leu Val Thr Lys Phe Glu Lys Asp His Met
1445 1450 1455

Asn Glu Ile Ser Ala Leu Ile Gly Asp Asp Asp Ile Asn Ser Phe Ile
1460 1465 1470

Thr Glu Phe Leu Leu Ile Glu Pro Arg Leu Phe Thr Ile Tyr Leu Gly

1475 1480 1485

Gln Cys Ala Ala Ile Asn Trp Ala Phe Asp Val His Tyr His Arg Pro
1490 1495 1500

Ser Gly Lys Tyr Gln Met Gly Glu Leu Leu Ser Ser Phe Leu Ser Arg
1505 1510 1515 1520

Met Ser Lys Gly Val Phe Lys Val Leu Val Asn Ala Leu Ser His Pro
1525 1530 1535

Lys Ile Tyr Lys Lys Phe Trp His Cys Gly Ile Ile Glu Pro Ile His
1540 1545 1550

Gly Pro Ser Leu Asp Ala Gln Asn Leu His Thr Thr Val Cys Asn Met
1555 1560 1565

Val Tyr Thr Cys Tyr Met Thr Tyr Leu Asp Leu Leu Leu Asn Glu Glu
1570 1575 1580

Leu Glu Glu Phe Thr Phe Leu Leu Cys Glu Ser Asp Glu Asp Val Val
1585 1590 1595 1600

Pro Asp Arg Phe Asp Asn Ile Gln Ala Lys His Leu Cys Val Leu Ala
1605 1610 1615

Asp Leu Tyr Cys Gln Pro Gly Thr Cys Pro Pro Ile Arg Gly Leu Arg
1620 1625 1630

Pro Val Glu Lys Cys Ala Val Leu Thr Asp His Ile Lys Ala Glu Ala
1635 1640 1645

Arg Leu Ser Pro Ala Gly Ser Ser Trp Asn Ile Asn Pro Ile Ile Val
1650 1655 1660

Asp His Tyr Ser Cys Ser Leu Thr Tyr Leu Arg Arg Gly Ser Ile Lys
1665 1670 1675 1680

Gln Ile Arg Leu Arg Val Asp Pro Gly Phe Ile Phe Asp Ala Leu Ala
1685 1690 1695

Glu Val Asn Val Ser Gln Pro Lys Val Gly Ser Asn Asn Ile Ser Asn
1700 1705 1710

Met Ser Ile Lys Asp Phe Arg Pro Pro His Asp Asp Val Ala Lys Leu
1715 1720 1725

Leu Lys Asp Ile Asn Thr Ser Lys His Asn Leu Pro Ile Ser Gly Gly
1730 1735 1740

Ser Leu Ala Asn Tyr Glu Ile His Ala Phe Arg Arg Ile Gly Leu Asn
1745 1750 1755 1760

Ser Ser Ala Cys Tyr Lys Ala Val Glu Ile Ser Thr Leu Ile Arg Arg
1765 1770 1775

Cys Leu Glu Pro Gly Glu Asp Gly Leu Phe Leu Gly Glu Gly Ser Gly
1780 1785 1790

Ser Met Leu Ile Thr Tyr Lys Glu Ile Leu Lys Leu Asn Lys Cys Phe
1795 1800 1805

Tyr Asn Ser Gly Val Ser Ala Asn Ser Arg Ser Gly Gln Arg Glu Leu
1810 1815 1820

Ala Pro Tyr Pro Ser Glu Val Gly Leu Val Glu His Arg Met Gly Val
1825 1830 1835 1840

Gly Asn Ile Val Lys Val Leu Phe Asn Gly Arg Pro Glu Val Thr Trp
1845 1850 1855

Val Gly Ser Ile Asp Cys Phe Asn Phe Ile Val Ser Asn Ile Pro Thr
1860 1865 1870

Ser Ser Val Gly Phe Ile His Ser Asp Ile Glu Thr Leu Pro Asn Lys
1875 1880 1885

Asp Thr Ile Glu Lys Leu Glu Glu Leu Ala Ala Ile Leu Ser Met Ala
1890 1895 1900

Leu Leu Leu Gly Lys Ile Gly Ser Ile Leu Val Ile Lys Leu Met Pro
1905 1910 1915 1920

Phe Ser Gly Asp Phe Val Gln Gly Phe Ile Ser Tyr Val Gly Ser His
1925 1930 1935

Tyr Arg Glu Val Asn Leu Val Tyr Pro Arg Tyr Ser Asn Phe Ile Ser
1940 1945 1950

Thr Glu Ser Tyr Leu Val Met Thr Asp Leu Lys Ala Asn Arg Leu Met
1955 1960 1965

Asn Pro Glu Lys Ile Lys Gln Gln Ile Ile Glu Ser Ser Val Arg Thr
1970 1975 1980

Ser Pro Gly Leu Ile Gly His Ile Leu Ser Ile Lys Gln Leu Ser Cys
1985 1990 1995 2000

Ile Gln Ala Ile Val Gly Gly Ala Val Ser Arg Gly Asp Ile Asn Pro
2005 2010 2015

Ile Leu Lys Lys Leu Thr Pro Ile Glu Gln Val Leu Ile Ser Cys Gly
2020 2025 2030

Leu Ala Ile Asn Gly Pro Lys Leu Cys Lys Glu Leu Ile His His Asp
2035 2040 2045

Val Ala Ser Gly Gln Asp Gly Leu Leu Asn Ser Ile Leu Ile Leu Tyr
2050 2055 2060

Arg Glu Leu Ala Arg Phe Lys Asp Asn Gln Arg Ser Gln Gln Gly Met
2065 2070 2075 2080

Phe His Ala Tyr Pro Val Leu Val Ser Ser Arg Gln Arg Glu Leu Val
2085 2090 2095

Ser Arg Ile Thr Arg Lys Phe Trp Gly His Ile Leu Leu Tyr Ser Gly
2100 2105 2110

Asn Arg Lys Leu Ile Asn Arg Phe Ile Gln Asn Leu Lys Ser Gly Tyr
2115 2120 2125

Leu Ile Leu Asp Leu His Gln Asn Ile Phe Val Lys Asn Leu Ser Lys
2130 2135 2140

Ser Glu Lys Gln Ile Ile Met Thr Gly Gly Leu Lys Arg Glu Trp Val
2145 2150 2155 2160

Phe Lys Val Thr Val Lys Glu Thr Lys Glu Trp Tyr Lys Leu Val Gly
2165 2170 2175

Tyr Ser Ala Leu Ile Lys Asp
2180

(2) INFORMATION FOR SEQ ID NO:9:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 15894 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

ACCAAACAAA GTTGGGTAAG GATAGTTCAA TCAATGATCA TCTTCTAGTG CACTTAGGAT 60

TCAAGATCCT ATTATCAGGG ACAAGAGCAG GATTAGGGAT ATCCGAGATG GCCACACTTT 120

TAAGGAGCTT AGCATTGTTC AAAAGAAACA AGGACAAACC ACCCATTACA TCAGGATCCG 180

GTGGAGCCAT CAGAGGAATC AAACACATTA TTATAGTACC AATCCCTGGA GATTCCTCAA 240

TTACCACTCG ATCCAGACTT CTGGACCGGT TGGTCAGGTT AATTGGAAAC CCGGATGTGA 300
GCGGGCCCAA ACTAACAGGG GCACTAATAG GTATATTATC CTTATTTGTG GAGTCTCCAG 360
GTCAATTGAT TCAGAGGATC ACCGATGACC CTGACGTTAG CATAAGGCTG TTAGAGGTTG 420
TCCAGAGTGA CCAGTCACAA TCTGGCCTTA CCTTCGCATC AAGAGGTACC AACATGGAGG 480
ATGAGGCGGA CCAATACTTT TCACATGATG ATCCAATTAG TAGTGATCAA TCCAGGTTCG 540
GATGGTTCGA GAACAAGGAA ATCTCAGATA TTGAAGTGCA AGACCCTGAG GGATTCAACA 600
TGATTCTGGG TACCATCCTA GCCCAAATTT GGGTCTTGCT CGCAAAGGCG GTTACGGCCC 660
CAGACACGGC AGCTGATTCG GAGCTAAGAA GGTGGATAAA GTACACCCAA CAAAGAAGGG 720
TGGTTGGTGA ATTTAGATTG GAGAGAAAAT GGTTGGATGT GGTGAGGAAC AGGATTGCCG 780
AGGACCTCTC CTTACGCCGA TTCATGGTCG CTCTAATCCT GGATATCAAG AGAACACCCG 840
GAAACAAACC CAGGATTGCT GAAATGATAT GTGACATTGA TACATATATC GTAGAGGCAG 900
GATTAGCCAG TTTTATCCTG ACTATTAAGT TTGGGATAGA AACTATGTAT CCTGCTCTTG 960
GACTGCATGA ATTTGCTGGT GAGTTATCCA CACTTGAGTC CTTGATGAAC CTTTACCAGC 1020
AAATGGGGGA AACTGCACCC TACATGGTAA TCCTGGAGAA CTCAATTCAG AACAAGTTCA 1080
GTGCAGGATC ATACCCTCTG CTCTGGAGCT ATGCCATGGG AGTAGGAGTG GAACTTGAAA 1140
ACTCCATGGG AGGTTTGAAC TTTGGCCGAT CTTACTTTGA TCCAGCATAT TTTAGATTAG 1200
GGCAAGAGAT GGTAAGGAGG TCAGCTGGAA AGGTCAGTTC CACATTGGCA TCTGAACTCG 1260
GTATCACTGC CGAGGATGCA AGGCTTGTTT CAGAGATTGC AATGCATACT ACTGAGGACA 1320
AGATCAGTAG AGCGGTTGGA CCCAGACAAG CCCAAGTATC ATTTCTACAC GGTGATCAAA 1380
GTGAGAATGA GCTACCGAGA TTGGGGGGCA AGGAAGATAG GAGGGTCAAA CAGAGTCGAG 1440
GAGAAGCCAG GGAGAGCTAC AGAGAAACCG GGCCCAGCAG AGCAAGTGAT GCGAGAGCTG 1500
CCCATCTTCC AACCGGCACA CCCCTAGACA TTGACACTGC AACGGAGTCC AGCCAAGATC 1560
CGCAGGACAG TCGAAGGTCA GCTGACGCCC TGCTTAGGCT GCAAGCCATG GCAGGAATCT 1620
CGGAAGAACA AGGCTCAGAC ACGGACACCC CTATAGTGTA CAATGACAGA AATCTTCTAG 1680
ACTAGGTGCG AGAGGCCGAG GGCCAGAACA ACATCCGCCT ACCCTCCATC ATTGTTATAA 1740
AAAACTTAGG AACCAGGTCC ACACAGCCGC CAGCCCATCA ACCATCCACT CCCACGATTG 1800

GAGCCAATGG CAGAAGAGCA GGCACGCCAT GTCAAAAACG GACTGGAATG CATCCGGGCT 1860

CTCAAGGCCG AGCCCATCGG CTCACTGGCC ATCGAGGAAG CTATGGCAGC ATGGTCAGAA 1920

ATATCAGACA ACCCAGGACA GGAGCGAGCC ACCTGCAGGG AAGAGAAGGC AGGCAGTTCG 1980

GGTCTCAGCA AACCATGCCT CTCAGCAATT GGATCAACTG AAGGCGGTGC ACCTCGCATC 2040

CGCGGTCAGG GACCTGGAGA GAGCGATGAC GACGCTGAAA CTTTGGGAAT CCCCCCAAGA 2100

AATCTCCAGG CATCAAGCAC TGGGTTACAG TGTTATTACG TTTATGATCA CAGCGGTGAA 2160

GCGGTTAAGG GAATCCAAGA TGCTGACTCT ATCATGGTTC AATCAGGCCT TGATGGTGAT 2220

AGCACCCTCT CAGGAGGAGA CAATGAATCT GAAAACAGCG ATGTGGATAT TGGCGAACCT 2280

GATACCGAGG GATATGCTAT CACTGACCGG GGATCTGCTC CCATCTCTAT GGGGTTCAGG 2340

GCTTCTGATG TTGAAACTGC AGAAGGAGGG GAGATCCACG AGCTCCTGAG ACTCCAATCC 2400

AGAGGCAACA ACTTTCCGAA GCTTGGGAAA ACTCTCAATG TTCCTCCGCC CCCGGACCCC 2460

GGTAGGGCCA GCACTTCCGG GACACCCATT AAAAAGGGCA CAGACGCGAG ATTAGCCTCA 2520

TTTGGAACGG AGATCGCGTC TTTATTGACA GGTGGTGCAA CCCAATGTGC TCGAAAGTCA 2580

CCCTCGGAAC CATCAGGGCC AGGTGCACCT GCGGGGAATG TCCCCGAGTG TGTGAGCAAT 2640

GCCGCACTGA TACAGGAGTG GACACCCGAA TCTGGTACCA CAATCTCCCC GAGATCCCAG 2700

AATAATGAAG AAGGGGGAGA CTATTATGAT GATGAGCTGT TCTCTGATGT CCAAGATATT 2760

AAAACAGCCT TGGCCAAAAT ACACGAGGAT AATCAGAAGA TAATCTCCAA GCTAGAATCA 2820

CTGCTGTTAT TGAAGGGAGA AGTTGAGTCA ATTAAGAAGC AGATCAACAG GCAAAATATC 2880

AGCATATCCA CCCTGGAAGG ACACCTCTCA AGCATCATGA TCGCCATTCC TGGACTTGGG 2940

AAGGATCCCA ACGACCCCAC TGCAGATGTC GAAATCAATC CCGACTTGAA ACCCATCATA 3000

GGCAGAGATT CAGGCCGAGC ACTGGCCGAA GTTCTCAAGA AACCCGTTGC CAGCCGACAA 3060

CTCCAAGGAA TGACAAATGG ACGGACCAGT TCCAGAGGAC AGCTGCTGAA GGAATTTCAG 3120

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TATATTAAAG AAAACTTTGA AAATACGAAG TTTCTATTCC CAGCTTTGTC TGGT 15894

(2) INFORMATION FOR SEQ ID NO:10:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2183 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

Met Asp Ser Leu Ser Val Asn Gln Ile Leu Tyr Pro Glu Val His Leu
1 5 10 15

Asp Ser Pro Ile Val Thr Asn Lys Ile Val Ala Ile Leu Glu Tyr Ala
20 25 30

Arg Val Pro His Ala Tyr Ser Leu Glu Asp Pro Thr Leu Cys Gln Asn
35 40 45

Ile Lys His Arg Leu Lys Asn Gly Phe Ser Asn Gln Met Ile Ile Asn
50 55 60

Asn Val Glu Val Gly Asn Val Ile Lys Ser Lys Leu Arg Ser Tyr Pro
65 70 75 80

Ala His Ser His Ile Pro Tyr Pro Asn Cys Asn Gln Asp Leu Phe Asn
85 90 95

Ile Glu Asp Lys Glu Ser Thr Arg Lys Ile Arg Glu Leu Leu Lys Lys
100 105 110

Gly Asn Ser Leu Tyr Ser Lys Val Ser Asp Lys Val Phe Gln Cys Leu
115 120 125

Arg Asp Thr Asn Ser Arg Leu Gly Leu Gly Ser Glu Leu Arg Glu Asp
130 135 140

Ile Lys Glu Lys Val Ile Asn Leu Gly Val Tyr Met His Ser Ser Gln
145 150 155 160

Trp Phe Glu Pro Phe Leu Phe Trp Phe Thr Val Lys Thr Glu Met Arg
165 170 175

Ser Val Ile Lys Ser Gln Thr His Thr Cys His Arg Arg Arg His Thr

180 185 190

Pro Val Phe Phe Thr Gly Ser Ser Val Glu Leu Leu Ile Ser Arg Asp
195 200 205

Leu Val Ala Ile Ile Ser Lys Glu Ser Gln His Val Tyr Tyr Leu Thr
210 215 220

Phe Glu Leu Val Leu Met Tyr Cys Asp Val Ile Glu Gly Arg Leu Met
225 230 235 240

Thr Glu Thr Ala Met Thr Ile Asp Ala Arg Tyr Thr Glu Leu Leu Gly
245 250 255

Arg Val Arg Tyr Met Trp Lys Leu Ile Asp Gly Phe Phe Pro Ala Leu
260 265 270

Gly Asn Pro Thr Tyr Gln Ile Val Ala Met Leu Glu Pro Leu Ser Leu
275 280 285

Ala Tyr Leu Gln Leu Arg Asp Ile Thr Val Glu Leu Arg Gly Ala Phe
290 295 300

Leu Asn His Cys Phe Thr Glu Ile His Asp Val Leu Asp Gln Asn Gly
305 310 315 320

Phe Ser Asp Glu Gly Thr Tyr His Glu Leu Ile Glu Ala Leu Asp Tyr
325 330 335

Ile Phe Ile Thr Asp Asp Ile His Leu Thr Gly Glu Ile Phe Ser Phe
340 345 350

Phe Arg Ser Phe Gly His Pro Arg Leu Glu Ala Val Thr Ala Ala Glu
355 360 365

Asn Val Arg Lys Tyr Met Asn Gln Pro Lys Val Ile Val Tyr Glu Thr
370 375 380

Leu Met Lys Gly His Ala Ile Phe Cys Gly Ile Ile Ile Asn Gly Tyr
385 390 395 400

Arg Asp Arg His Gly Gly Ser Trp Pro Pro Leu Thr Leu Pro Leu His
405 410 415

Ala Ala Asp Thr Ile Arg Asn Ala Gln Ala Ser Gly Glu Gly Leu Thr
420 425 430

His Glu Gln Cys Val Asp Asn Trp Lys Ser Phe Ala Gly Val Lys Phe
435 440 445

Gly Cys Phe Met Pro Leu Ser Leu Asp Ser Asp Leu Thr Met Tyr Leu
450 455 460

Lys Asp Lys Ala Leu Ala Ala Leu Gln Arg Glu Trp Asp Ser Val Tyr
465   470   475   480

Pro Lys Glu Phe Leu Arg Tyr Asp Pro Pro Lys Gly Thr Gly Ser Arg
                485   490   495

Arg Leu Val Asp Val Phe Leu Asn Asp Ser Ser Phe Asp Pro Tyr Asp
            500   505   510

Val Ile Met Tyr Val Val Ser Gly Ala Tyr Leu His Asp Pro Glu Phe
        515   520   525

Asn Leu Ser Tyr Ser Leu Lys Glu Lys Glu Ile Lys Glu Thr Gly Arg
    530   535   540

Leu Phe Ala Lys Met Thr Tyr Lys Met Arg Ala Cys Gln Val Ile Ala
545   550   555   560

Glu Asn Leu Ile Ser Asn Gly Ile Gly Lys Tyr Phe Lys Asp Asn Gly
                565   570   575

Met Ala Lys Asp Glu His Asp Leu Thr Lys Ala Leu His Thr Leu Ala
            580   585   590

Val Ser Gly Val Pro Lys Asp Leu Lys Glu Ser His Arg Gly Gly Pro
        595   600   605

Val Leu Lys Thr Tyr Ser Arg Ser Pro Val His Thr Ser Thr Arg Asn
    610   615   620

Val Arg Ala Ala Lys Gly Phe Ile Gly Phe Pro Gln Val Ile Arg Gln
625   630   635   640

Asp Gln Asp Thr Asp His Pro Glu Asn Met Glu Ala Tyr Glu Thr Val
                645   650   655

Ser Ala Phe Ile Thr Thr Asp Leu Lys Lys Tyr Cys Leu Asn Trp Arg
            660   665   670

Tyr Glu Thr Ile Ser Leu Phe Ala Gln Arg Leu Asn Glu Ile Tyr Gly
        675   680   685

Leu Pro Ser Phe Phe Gln Trp Leu His Lys Arg Leu Glu Thr Ser Val
    690   695   700

Leu Tyr Val Ser Asp Pro His Cys Pro Pro Asp Leu Asp Ala His Ile
705   710   715   720

Pro Leu Tyr Lys Val Pro Asn Asp Gln Ile Phe Ile Lys Tyr Pro Met
                725   730   735

Gly Gly Ile Glu Gly Tyr Cys Gln Lys Leu Trp Thr Ile Ser Thr Ile
740 745 750

Pro Tyr Leu Tyr Leu Ala Ala Tyr Glu Ser Gly Val Arg Ile Ala Ser
755 760 765

Leu Val Gln Gly Asp Asn Gln Thr Ile Ala Val Thr Lys Arg Val Pro
770 775 780

Ser Thr Trp Pro Tyr Asn Leu Lys Lys Arg Glu Ala Ala Arg Val Thr
785 790 795 800

Arg Asp Tyr Phe Val Ile Leu Arg Gln Arg Leu His Asp Ile Gly His
805 810 815

His Leu Lys Ala Asn Glu Thr Ile Val Ser Ser His Phe Phe Val Tyr
820 825 830

Ser Lys Gly Ile Tyr Tyr Asp Gly Leu Leu Val Ser Gln Ser Leu Lys
835 840 845

Ser Ile Ala Arg Cys Val Phe Trp Ser Glu Thr Ile Val Asp Glu Thr
850 855 860

Arg Ala Ala Cys Ser Asn Ile Ala Thr Thr Met Ala Lys Ser Ile Glu
865 870 875 880

Arg Gly Tyr Asp Arg Tyr Leu Ala Tyr Ser Leu Asn Val Leu Lys Val
885 890 895

Ile Gln Gln Ile Leu Ile Ser Leu Gly Phe Thr Ile Asn Ser Thr Met
900 905 910

Thr Arg Asp Val Val Ile Pro Leu Leu Thr Asn Asn Asp Leu Leu Ile
915 920 925

Arg Met Ala Leu Leu Pro Ala Pro Ile Gly Gly Met Asn Tyr Leu Asn
930 935 940

Met Ser Arg Leu Phe Val Arg Asn Ile Gly Asp Pro Val Thr Ser Ser
945 950 955 960

Ile Ala Asp Leu Lys Arg Met Ile Leu Ala Ser Leu Met Pro Glu Glu
965 970 975

Thr Leu His Gln Val Met Thr Gln Gln Pro Gly Asp Ser Ser Phe Leu
980 985 990

Asp Trp Ala Ser Asp Pro Tyr Ser Ala Asn Leu Val Cys Val Gln Ser
995 1000 1005

Ile Thr Arg Leu Leu Lys Asn Ile Thr Ala Arg Phe Val Leu Ile His

1010 1015 1020

Ser Pro Asn Pro Met Leu Lys Gly Leu Phe His Asp Asp Ser Lys Glu
1025 1030 1035 1040

Glu Asp Glu Gly Leu Ala Ala Phe Leu Met Asp Arg His Ile Ile Val
1045 1050 1055

Pro Arg Ala Ala His Glu Ile Leu Asp His Ser Val Thr Gly Ala Arg
1060 1065 1070

Glu Ser Ile Ala Gly Met Leu Asp Thr Thr Lys Gly Leu Ile Arg Ala
1075 1080 1085

Ser Met Arg Lys Gly Gly Leu Thr Ser Arg Val Ile Thr Arg Leu Ser
1090 1095 1100

Asn Tyr Asp Tyr Glu Gln Phe Arg Ala Gly Met Val Leu Leu Thr Gly
1105 1110 1115 1120

Arg Lys Arg Asn Val Leu Ile Asp Lys Glu Ser Cys Ser Val Gln Leu
1125 1130 1135

Ala Arg Ala Leu Arg Ser His Met Trp Ala Arg Leu Ala Arg Gly Arg
1140 1145 1150

Pro Ile Tyr Gly Leu Glu Val Pro Asp Val Leu Glu Ser Met Arg Gly
1155 1160 1165

His Leu Ile Arg Arg His Glu Thr Cys Val Ile Cys Glu Cys Gly Ser
1170 1175 1180

Val Asn Tyr Gly Trp Phe Phe Val Pro Ser Gly Cys Gln Leu Asp Asp
1185 1190 1195 1200

Ile Asp Lys Glu Thr Ser Ser Leu Arg Val Pro Tyr Ile Gly Ser Thr
1205 1210 1215

Thr Asp Glu Arg Thr Asp Met Lys Leu Ala Phe Val Arg Ala Pro Ser
1220 1225 1230

Arg Ser Leu Arg Ser Ala Val Arg Ile Ala Thr Val Tyr Ser Trp Ala
1235 1240 1245

Tyr Gly Asp Asp Asp Ser Ser Trp Asn Glu Ala Trp Leu Leu Ala Arg
1250 1255 1260

Gln Arg Ala Asn Val Ser Leu Glu Glu Leu Arg Val Ile Thr Pro Ile
1265 1270 1275 1280

Ser Thr Ser Thr Asn Leu Ala His Arg Leu Arg Asp Arg Ser Thr Gln
1285 1290 1295

Val Lys Tyr Ser Gly Thr Ser Leu Val Arg Val Ala Arg Tyr Thr Thr
1300 1305 1310

Ile Ser Asn Asp Asn Leu Ser Phe Val Ile Ser Asp Lys Lys Val Asp
1315 1320 1325

Thr Asn Phe Ile Tyr Gln Gln Gly Met Leu Leu Gly Leu Gly Val Leu
1330 1335 1340

Glu Thr Leu Phe Arg Leu Glu Lys Asp Thr Gly Ser Ser Asn Thr Val
1345 1350 1355 1360

Leu His Leu His Val Glu Thr Asp Cys Cys Val Ile Pro Met Ile Asp
1365 1370 1375

His Pro Arg Ile Pro Ser Ser Arg Lys Leu Glu Leu Arg Ala Glu Leu
1380 1385 1390

Cys Thr Asn Pro Leu Ile Tyr Asp Asn Ala Pro Leu Ile Asp Arg Asp
1395 1400 1405

Ala Thr Arg Leu Tyr Thr Gln Ser His Arg Arg His Leu Val Glu Phe
1410 1415 1420

Val Thr Trp Ser Thr Pro Gln Leu Tyr His Ile Leu Ala Lys Ser Thr
1425 1430 1435 1440

Ala Leu Ser Met Ile Asp Leu Val Thr Lys Phe Glu Lys Asp His Met
1445 1450 1455

Asn Glu Ile Ser Ala Leu Ile Gly Asp Asp Asp Ile Asn Ser Phe Ile
1460 1465 1470

Thr Glu Phe Leu Leu Ile Glu Pro Arg Leu Phe Thr Ile Tyr Leu Gly
1475 1480 1485

Gln Cys Ala Ala Ile Asn Trp Ala Phe Asp Val His Tyr His Arg Pro
1490 1495 1500

Ser Gly Lys Tyr Gln Met Gly Glu Leu Leu Ser Ser Phe Leu Ser Arg
1505 1510 1515 1520

Met Ser Lys Gly Val Phe Lys Val Leu Val Asn Ala Leu Ser His Pro
1525 1530 1535

Lys Ile Tyr Lys Lys Phe Trp His Cys Gly Ile Ile Glu Pro Ile His
1540 1545 1550

Gly Pro Ser Leu Asp Ala Gln Asn Leu His Thr Thr Val Cys Asn Met
1555 1560 1565

Val Tyr Thr Cys Tyr Met Thr Tyr Leu Asp Leu Leu Leu Asn Glu Glu
1570 1575 1580

Leu Glu Glu Phe Thr Phe Leu Leu Cys Glu Ser Asp Glu Asp Val Val
1585 1590 1595 1600

Pro Asp Arg Phe Asp Asn Ile Gln Ala Lys His Leu Cys Val Leu Ala
1605 1610 1615

Asp Leu Tyr Cys Gln Pro Gly Thr Cys Pro Pro Ile Arg Gly Leu Arg
1620 1625 1630

Pro Val Glu Lys Cys Ala Val Leu Thr Asp His Ile Lys Ala Glu Ala
1635 1640 1645

Met Leu Ser Pro Ala Gly Ser Ser Trp Asn Ile Asn Pro Ile Ile Val
1650 1655 1660

Asp His Tyr Ser Cys Ser Leu Thr Tyr Leu Arg Arg Gly Ser Ile Lys
1665 1670 1675 1680

Gln Ile Arg Leu Arg Val Asp Pro Gly Phe Ile Phe Asp Ala Leu Ala
1685 1690 1695

Glu Val Asn Val Ser Gln Pro Lys Ile Gly Ser Asn Asn Ile Ser Asn
1700 1705 1710

Met Ser Ile Lys Ala Phe Arg Pro Pro His Asp Asp Val Ala Lys Leu
1715 1720 1725

Leu Lys Asp Ile Asn Thr Ser Lys His Asn Leu Pro Ile Ser Gly Gly
1730 1735 1740

Asn Leu Ala Asn Tyr Glu Ile His Ala Phe Arg Arg Ile Gly Leu Asn
1745 1750 1755 1760

Ser Ser Ala Cys Tyr Lys Ala Val Glu Ile Ser Thr Leu Ile Arg Arg
1765 1770 1775

Cys Leu Glu Pro Gly Glu Asp Gly Leu Phe Leu Gly Glu Gly Ser Gly
1780 1785 1790

Ser Met Leu Ile Thr Tyr Lys Glu Ile Leu Lys Leu Asn Lys Cys Phe
1795 1800 1805

Tyr Asn Ser Gly Val Ser Ala Asn Ser Arg Ser Gly Gln Arg Glu Leu
1810 1815 1820

Ala Pro Tyr Pro Ser Glu Val Gly Leu Val Glu His Arg Met Gly Val
1825 1830 1835 1840

Gly Asn Ile Val Lys Val Leu Phe Asn Gly Arg Pro Glu Val Thr Trp

1845 1850 1855

Val Gly Ser Val Asp Cys Phe Asn Phe Ile Val Ser Asn Ile Pro Thr
1860 1865 1870

Ser Ser Val Gly Phe Ile His Ser Asp Ile Glu Thr Leu Pro Asp Lys
1875 1880 1885

Asp Thr Ile Glu Lys Leu Glu Glu Leu Ala Ala Ile Leu Ser Met Ala
1890 1895 1900

Leu Leu Leu Gly Lys Ile Gly Ser Ile Leu Val Ile Lys Leu Met Pro
1905 1910 1915 1920

Phe Ser Gly Asp Phe Val Gln Gly Phe Ile Ser Tyr Val Gly Ser His
1925 1930 1935

Tyr Arg Glu Val Asn Leu Val Tyr Pro Arg Tyr Ser Asn Phe Ile Ser
1940 1945 1950

Thr Glu Ser Tyr Leu Val Met Thr Asp Leu Lys Ala Asn Arg Leu Met
1955 1960 1965

Asn Pro Glu Lys Ile Lys Gln Gln Ile Ile Glu Ser Ser Val Arg Thr
1970 1975 1980

Ser Pro Gly Leu Ile Gly His Ile Leu Ser Ile Lys Gln Leu Ser Cys
1985 1990 1995 2000

Ile Gln Ala Ile Val Gly Asp Ala Val Ser Arg Gly Asp Ile Asn Pro
2005 2010 2015

Thr Leu Lys Lys Leu Thr Pro Ile Glu Gln Val Leu Ile Asn Cys Gly
2020 2025 2030

Leu Ala Ile Asn Gly Pro Lys Leu Cys Lys Glu Leu Ile His His Asp
2035 2040 2045

Val Ala Ser Gly Gln Asp Gly Leu Leu Asn Ser Ile Leu Ile Leu Tyr
2050 2055 2060

Arg Glu Leu Ala Arg Phe Lys Asp Asn Gln Arg Ser Gln Gln Gly Met
2065 2070 2075 2080

Phe His Ala Tyr Pro Val Leu Val Ser Ser Arg Gln Arg Glu Leu Ile
2085 2090 2095

Ser Arg Ile Thr Arg Lys Phe Trp Gly His Ile Leu Leu Tyr Ser Gly
2100 2105 2110

Asn Arg Lys Leu Ile Asn Lys Phe Ile Gln Asn Leu Lys Ser Gly Tyr
2115 2120 2125

Leu Ile Leu Asp Leu His Gln Asn Ile Phe Val Lys Asn Leu Ser Lys
    2130 2135 2140

Ser Glu Lys Gln Ile Ile Met Thr Gly Gly Leu Lys Arg Glu Trp Val
2145 2150 2155 2160

Phe Lys Val Thr Val Lys Glu Thr Lys Glu Trp Tyr Lys Leu Val Gly
    2165 2170 2175

Tyr Ser Ala Leu Ile Lys Asp
    2180

(2) INFORMATION FOR SEQ ID NO:11:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 15894 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

ACCAAACAAA GTTGGGTAAG GATAGTTCAA TCAATGATCA TCTTCTAGTG CACTTAGGAT 60

TCAAGATCCT ATTATCAGGG ACAAGAGCAG GATTAGGGAT ATCCGAGATG GCCACACTTT 120

TAAGGAGCTT AGCATTGTTC AAAAGAAACA AGGACAAACC ACCCATTACA TCAGGATCCG 180

GTGGAGCCAT CAGAGGAATC AAACACATTA TTATAGTACC AATCCCTGGA GATTCCTCAA 240

TTACCACTCG ATCCAGACTT CTGGACCGGT TGGTGAGGTT AATTGGAAAC CCGGATGTGA 300

GCGGGCCCAA ACTAACAGGG GCACTAATAG GTATATTATC CTTATTTGTG GAGTCTCCAG 360

GTCAATTGAT TCAGAGGATC ACCGATGACC CTGACGTTAG CATAAGGCTG TTAGAGGTTG 420

TCCAGAGTGA CCAGTCACAA TCTGGCCTTA CCTTCGCATC AAGAGGTACC AACATGGAGG 480

ATGAGGCGGA CCAATACTTT TCACATGATG ATCCAATTAG TAGTGATCAA TCCAGGTTCG 540

GATGGTTCGG GAACAAGGAA ATCTCAGATA TTGAAGTGCA AGACCCTGAG GGATTCAACA 600

TGATTCTGGG TACCATCCTA GCCCAAATTT GGGTCTTGCT CGCAAAGGCG GTTACGGCCC 660

CAGACACGGC AGCTGATTCG GAGCTAAGAA GGTGGATAAA GTACACCCAA CAAAGAAGGG 720

TAGTTGGTGA ATTTAGATTG GAGAGAAAAT GGTTGGATGT GGTGAGGAAC AGGATTGCCG 780

AGGACCTCTC CTTACGCCGA TTCATGGTCG CTCTAATCCT GGATATCAAG AGAACACCCG 840

GAAACAAACC CAGGATTGCT GAAATGATAT GTGACATTGA TACATATATC GTAGAGGCAG 900

GATTAGCCAG TTTTATCCTG ACTATTAAGT TTGGGATAGA AACTATGTAT CCTGCTCTTG 960

GACTGCATGA ATTTGCTGGT GAGTTATCCA CACTTGAGTC CTTGATGAAC CTTTACCAGC 1020

AAATGGGGGA AACTGCACCC TACATGGTAA TCCTGGAGAA CTCAATTCAG AACAAGTTCA 1080

GTGCAGGATC ATACCCTCTG CTCTGGAGCT ATGCCATGGG AGTAGGAGTG GAACTTGAAA 1140

ACTCCATGGG AGGTTTGAAC TTTGGCCGAT CTTACTTTGA TCCAGCATAT TTTAGATTAG 1200

GGCAAGAGAT GGTAAGGAGG TCAGCTGGAA AGGTCAGTTC CACATTGGCA TCTGAACTCG 1260

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CCCATCTTCC AACCGGCACA CCCCTAGACA TTGACACTGC AACGGAGTCC AGCCAAGATC 1560

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CGGAAGAACA AGGCTCAGAC ACGGACACCC CTATAGTGTA CAATGACAGA AATCTTCTAG 1680

ACTAGGTGCG AGAGGCCGAG GGCCAGAACA ACATCCGCCT ACCATCCATC ATTGTTATAA 1740

AAAACTTAGG AACCAGGTCC ACACAGCCGC CAGCCCATCA ACCATCCACT CCCACGATTG 1800

GAGCCAATGG CAGAAGAGCA GGCACGCCAT GTCAAAAACG GACTGGAATG CATCCGGGCT 1860

CTCAAGGCCG AGCCCATCGG CTCACTGGCC ATCGAGGAAG CTATGGCAGC ATGGTCAGAA 1920

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AAGGATCCCA ACGACCCCAC TGCAGATGTC GAAATCAATC CCGACTTGAA ACCCATCATA 3000

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GCATCACGCA GTGTAATCCG CTCCATTATA AAATCCAGCC GGCTAGAGGA GGATCGGAAG 3240

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GCCTATAAAG GGGGTCCCCA TCGAATTACA AGTGGAATGC TTCACATGGG ACCAAAAACT 9000
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GTGAAATAGA CATCAGAATT AAGAAAAACG TAGGGTCCAA GTGGTTCCCC GTTATGGACT 9240
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TAAACAATGT GGAAGTTGGG AATGTCATCA AGTCCAAGCT TAGGAGTTAT CCGGCCCACT 9480
CTCATATTCC ATATCCAAAT TGTAATCAGG ATTTATTTAA CATAGAAGAC AAAGAGTCAA 9540
CGAGGAAGAT CCGTGAACTC CTCAAAAAGG GGAATTCGCT GTACTCCAAA GTCAGTGATA 9600
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CCCATACTTG CCATAGGAGG AGACACACAC CTGTATTCTT CACTGGTAGT TCAGTTGAGT 9840
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TGGAGCCTCT TTCACTTGCT TACCTGCAGC TGAGGGATAT AACAGTAGAA CTCAGAGGTG 10140

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ATGAAGGTAC TTATCATGAG TTAACTGAAG CTCTAGATTA CATTTTCATA ACTGATGACA 10260

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CCAAGTCAGA GAAACAGATT ATTATGACGG GGGGTTTGAA ACGTGAGTGG GTTTTTAAGG 15720

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ACTAATTGGT TGAACTCCGG AACCCTAATC CTGCCCTAGG TGGTTAGGCA TTATTTGCAA 15840

TATATTAAAG AAAACTTTGA AAATACGAAG TTTCTATTCC CAGCTTTGTC TGGT 15894

(2) INFORMATION FOR SEQ ID NO:12:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2183 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

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Met Asp Ser Leu Ser Val Asn Gln Ile Leu Tyr Pro Glu Val His Leu
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Asp Ser Pro Ile Val Thr Asn Lys Ile Val Ala Ile Leu Glu Tyr Ala
            20                  25                  30

Arg Val Pro His Ala Tyr Ser Leu Glu Asp Pro Thr Leu Cys Gln Asn
        35                  40                  45

Ile Lys His Arg Leu Lys Asn Gly Phe Ser Asn Gln Met Ile Ile Asn
    50                  55                  60

Asn Val Glu Val Gly Asn Val Ile Lys Ser Lys Leu Arg Ser Tyr Pro
65                  70                  75                  80

Ala His Ser His Ile Pro Tyr Pro Asn Cys Asn Gln Asp Leu Phe Asn
                85                  90                  95

Ile Glu Asp Lys Glu Ser Thr Arg Lys Ile Arg Glu Leu Leu Lys Lys
            100                 105                 110

Gly Asn Ser Leu Tyr Ser Lys Val Ser Asp Lys Val Phe Gln Cys Leu
        115                 120                 125

Arg Asp Thr Asn Ser Arg Leu Gly Leu Gly Ser Glu Leu Arg Glu Asp
    130                 135                 140

Ile Lys Glu Lys Val Ile Asn Leu Gly Val Tyr Met His Ser Ser Gln
145                 150                 155                 160

Trp Phe Glu Pro Phe Leu Phe Trp Phe Thr Val Lys Thr Glu Met Arg
                165                 170                 175

Ser Val Ile Lys Ser Gln Thr His Thr Cys His Arg Arg Arg His Thr
            180                 185                 190

Pro Val Phe Phe Thr Gly Ser Ser Val Glu Leu Leu Ile Ser Arg Asp
        195                 200                 205

Leu Val Ala Ile Ile Ser Lys Glu Ser Gln His Val Tyr Tyr Leu Thr
    210                 215                 220

Phe Glu Leu Val Leu Met Tyr Cys Asp Val Ile Glu Gly Arg Leu Met
225                 230                 235                 240

Thr Glu Thr Ala Met Thr Ile Asp Ala Arg Tyr Thr Glu Leu Leu Gly
                245                 250                 255

Arg Val Arg Tyr Met Trp Lys Leu Ile Asp Gly Phe Phe Pro Ala Leu
            260                 265                 270
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Gly Asn Pro Thr Tyr Gln Ile Val Ala Met Leu Glu Pro Leu Ser Leu
275 280 285

Ala Tyr Leu Gln Leu Arg Asp Ile Thr Val Glu Leu Arg Gly Ala Phe
290 295 300

Leu Asn His Cys Phe Thr Glu Ile His Asp Val Leu Asp Gln Asn Gly
305 310 315 320

Phe Ser Asp Glu Gly Thr Tyr His Glu Leu Thr Glu Ala Leu Asp Tyr
325 330 335

Ile Phe Ile Thr Asp Asp Ile His Leu Thr Gly Glu Ile Phe Ser Phe
340 345 350

Phe Arg Ser Phe Gly His Pro Arg Leu Glu Ala Val Thr Ala Ala Glu
355 360 365

Asn Val Arg Lys Tyr Met Asn Gln Pro Lys Val Ile Val Tyr Glu Thr
370 375 380

Leu Met Lys Gly His Ala Ile Phe Cys Gly Ile Ile Ile Asn Gly Tyr
385 390 395 400

Arg Asp Arg His Gly Gly Ser Trp Pro Pro Leu Thr Leu Pro Leu His
405 410 415

Ala Ala Asp Thr Ile Arg Asn Ala Gln Ala Ser Gly Glu Gly Leu Thr
420 425 430

His Glu Gln Cys Val Asp Asn Trp Lys Ser Phe Ala Gly Val Lys Phe
435 440 445

Gly Cys Phe Met Pro Leu Ser Leu Asp Ser Asp Leu Thr Met Tyr Leu
450 455 460

Lys Asp Lys Ala Leu Ala Ala Leu Gln Arg Glu Trp Asp Ser Val Tyr
465 470 475 480

Pro Lys Glu Phe Leu Arg Tyr Asp Pro Pro Lys Gly Thr Gly Ser Arg
485 490 495

Arg Leu Val Asp Val Phe Leu Asn Asp Ser Ser Phe Asp Pro Tyr Asp
500 505 510

Val Ile Met Tyr Val Val Ser Gly Ala Tyr Leu His Asp Pro Glu Phe
515 520 525

Asn Leu Ser Tyr Ser Leu Lys Glu Lys Glu Ile Lys Glu Thr Gly Arg
530 535 540

Leu Phe Ala Lys Met Thr Tyr Lys Met Arg Ala Cys Gln Val Ile Ala

545 550 555 560

Glu Asn Leu Ile Ser Asn Gly Ile Gly Lys Tyr Phe Lys Asp Asn Gly
565 570 575

Met Ala Lys Asp Glu His Asp Leu Thr Lys Ala Leu His Thr Leu Ala
580 585 590

Val Ser Gly Val Pro Lys Asp Leu Lys Glu Ser His Arg Gly Gly Pro
595 600 605

Val Leu Lys Thr Tyr Ser Arg Ser Pro Val His Thr Ser Thr Arg Asn
610 615 620

Val Arg Ala Ala Lys Gly Phe Ile Gly Phe Pro Gln Val Ile Arg Gln
625 630 635 640

Asp Gln Asp Thr Asp His Pro Glu Asn Met Glu Ala Tyr Glu Thr Val
645 650 655

Ser Ala Phe Ile Thr Thr Asp Leu Lys Lys Tyr Cys Leu Asn Trp Arg
660 665 670

Tyr Glu Thr Ile Ser Leu Phe Ala Gln Arg Leu Asn Glu Ile Tyr Gly
675 680 685

Leu Pro Ser Phe Phe Gln Trp Leu His Lys Arg Leu Glu Thr Ser Val
690 695 700

Leu Tyr Val Ser Asp Pro His Cys Pro Pro Asp Leu Asp Ala His Ile
705 710 715 720

Pro Leu Tyr Lys Val Pro Asn Asp Gln Ile Phe Ile Lys Tyr Pro Met
725 730 735

Gly Gly Ile Glu Gly Tyr Cys Gln Lys Leu Trp Thr Ile Ser Thr Ile
740 745 750

Pro Tyr Leu Tyr Leu Ala Ala Tyr Glu Ser Gly Val Arg Ile Ala Ser
755 760 765

Leu Val Gln Gly Asp Asn Gln Thr Ile Ala Val Thr Lys Arg Val Pro
770 775 780

Ser Thr Trp Pro Tyr Asn Leu Lys Lys Arg Glu Ala Ala Arg Val Thr
785 790 795 800

Arg Asp Tyr Phe Val Ile Leu Arg Gln Arg Leu His Asp Ile Gly His
805 810 815

His Leu Lys Ala Asn Glu Thr Ile Val Ser Ser His Phe Phe Val Tyr
820 825 830

Ser Lys Gly Ile Tyr Tyr Asp Gly Leu Leu Val Ser Gln Ser Leu Lys
835 840 845

Ser Ile Ala Arg Cys Val Phe Trp Ser Glu Thr Ile Val Asp Glu Thr
850 855 860

Arg Ala Ala Cys Ser Asn Ile Ala Thr Thr Met Ala Lys Ser Ile Glu
865 870 875 880

Arg Gly Tyr Asp Arg Tyr Leu Ala Tyr Ser Leu Asn Val Leu Lys Val
885 890 895

Ile Gln Gln Ile Leu Ile Ser Leu Gly Phe Thr Ile Asn Ser Thr Met
900 905 910

Thr Arg Asp Val Val Ile Pro Leu Leu Thr Asn Asn Asp Leu Leu Ile
915 920 925

Arg Met Ala Leu Leu Pro Ala Pro Ile Gly Gly Met Asn Tyr Leu Asn
930 935 940

Met Ser Arg Leu Phe Val Arg Asn Ile Gly Asp Pro Val Thr Ser Ser
945 950 955 960

Ile Ala Asp Leu Lys Arg Met Ile Leu Ala Ser Leu Met Pro Glu Glu
965 970 975

Thr Leu His Gln Val Met Thr Gln Gln Pro Gly Asp Ser Ser Phe Leu
980 985 990

Asp Trp Ala Ser Asp Pro Tyr Ser Ala Asn Leu Val Cys Val Gln Ser
995 1000 1005

Ile Thr Arg Leu Leu Lys Asn Ile Thr Ala Arg Phe Val Leu Ile His
1010 1015 1020

Ser Pro Asn Pro Met Leu Lys Gly Leu Phe His Asp Asp Ser Lys Glu
1025 1030 1035 1040

Glu Asp Glu Gly Leu Ala Ala Phe Leu Met Asp Arg His Ile Ile Val
1045 1050 1055

Pro Arg Ala Ala His Glu Ile Leu Asp His Ser Val Thr Gly Ala Arg
1060 1065 1070

Glu Ser Ile Ala Gly Met Leu Asp Thr Thr Lys Gly Leu Ile Arg Ala
1075 1080 1085

Ser Met Arg Lys Gly Gly Leu Thr Ser Arg Val Ile Thr Arg Leu Ser
1090 1095 1100

Asn Tyr Asp Tyr Glu Gln Phe Arg Ala Gly Met Val Leu Leu Thr Gly
1105 1110 1115 1120

Arg Lys Arg Asn Val Leu Ile Asp Lys Glu Ser Cys Ser Val Gln Leu
1125 1130 1135

Ala Arg Ala Leu Arg Ser His Met Trp Ala Arg Leu Ala Arg Gly Arg
1140 1145 1150

Pro Ile Tyr Gly Leu Glu Val Pro Asp Val Leu Glu Ser Met Arg Gly
1155 1160 1165

His Leu Ile Arg Arg His Glu Thr Cys Val Ile Cys Glu Cys Gly Ser
1170 1175 1180

Val Asn Tyr Gly Trp Phe Phe Val Pro Ser Gly Cys Gln Leu Asp Asp
1185 1190 1195 1200

Ile Asp Lys Glu Thr Ser Ser Leu Arg Val Pro Tyr Ile Gly Ser Thr
1205 1210 1215

Thr Asp Glu Arg Thr Asp Met Lys Leu Ala Phe Val Arg Ala Pro Ser
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Arg Ser Leu Arg Ser Ala Val Arg Ile Ala Thr Val Tyr Ser Trp Ala
1235 1240 1245

Tyr Gly Asp Asp Asp Ser Ser Trp Asn Glu Ala Trp Leu Leu Ala Arg
1250 1255 1260

Gln Arg Ala Asn Val Ser Leu Glu Glu Leu Arg Val Ile Thr Pro Ile
1265 1270 1275 1280

Ser Thr Ser Thr Asn Leu Ala His Arg Leu Arg Asp Arg Ser Thr Gln
1285 1290 1295

Val Lys Tyr Ser Gly Thr Ser Leu Val Arg Val Ala Arg Tyr Thr Thr
1300 1305 1310

Ile Ser Asn Asp Asn Leu Ser Phe Val Ile Ser Asp Lys Lys Val Asp
1315 1320 1325

Thr Asn Phe Ile Tyr Gln Gln Gly Met Leu Leu Gly Leu Gly Val Leu
1330 1335 1340

Glu Thr Leu Phe Arg Leu Glu Lys Asp Thr Gly Ser Ser Asn Thr Val
1345 1350 1355 1360

Leu His Leu His Val Glu Thr Asp Cys Cys Val Ile Pro Met Ile Asp
1365 1370 1375

His Pro Arg Ile Pro Ser Ser Arg Lys Leu Glu Leu Arg Ala Glu Leu

1380 1385 1390

Cys Thr Asn Pro Leu Ile Tyr Asp Asn Ala Pro Leu Ile Asp Arg Asp
1395 1400 1405

Ala Thr Arg Leu Tyr Thr Gln Ser His Arg Arg His Leu Val Glu Phe
1410 1415 1420

Val Thr Trp Ser Thr Pro Gln Leu Tyr His Ile Leu Ala Lys Ser Thr
1425 1430 1435 1440

Ala Leu Ser Met Ile Asp Leu Val Thr Lys Phe Glu Lys Asp His Met
1445 1450 1455

Asn Glu Ile Ser Ala Leu Ile Gly Asp Asp Asp Ile Asn Ser Phe Ile
1460 1465 1470

Thr Glu Phe Leu Leu Ile Glu Pro Arg Leu Phe Thr Ile Tyr Leu Gly
1475 1480 1485

Gln Cys Ala Ala Ile Asn Trp Ala Phe Asp Val His Tyr His Arg Pro
1490 1495 1500

Ser Gly Lys Tyr Gln Met Gly Glu Leu Leu Ser Ser Phe Leu Ser Arg
1505 1510 1515 1520

Met Ser Lys Gly Val Phe Lys Val Leu Val Asn Ala Leu Ser His Pro
1525 1530 1535

Lys Ile Tyr Lys Lys Phe Trp His Cys Gly Ile Ile Glu Pro Ile His
1540 1545 1550

Gly Pro Ser Leu Asp Ala Gln Asn Leu His Thr Thr Val Cys Asn Met
1555 1560 1565

Val Tyr Thr Cys Tyr Met Thr Tyr Leu Asp Leu Leu Leu Asn Glu Glu
1570 1575 1580

Leu Glu Glu Phe Thr Phe Leu Leu Cys Glu Ser Asp Glu Asp Val Val
1585 1590 1595 1600

Pro Asp Arg Phe Asp Asn Ile Gln Ala Lys His Leu Cys Val Leu Ala
1605 1610 1615

Asp Leu Tyr Cys Gln Pro Gly Thr Cys Pro Pro Ile Arg Gly Leu Arg
1620 1625 1630

Pro Val Glu Lys Cys Ala Val Leu Thr Asp His Ile Lys Ala Glu Ala
1635 1640 1645

Met Leu Ser Pro Ala Gly Ser Ser Trp Asn Ile Asn Pro Ile Ile Val
1650 1655 1660

Asp His Tyr Ser Cys Ser Leu Thr Tyr Leu Arg Arg Gly Ser Ile Lys
1665 1670 1675 1680

Gln Ile Arg Leu Arg Val Asp Pro Gly Phe Ile Phe Asp Ala Leu Ala
1685 1690 1695

Glu Val Asn Val Ser Gln Pro Lys Ile Gly Ser Asn Asn Ile Ser Asn
1700 1705 1710

Met Ser Ile Lys Ala Phe Arg Pro Pro His Asp Asp Val Ala Lys Leu
1715 1720 1725

Leu Lys Asp Ile Asn Thr Ser Lys His Asn Leu Pro Ile Ser Gly Gly
1730 1735 1740

Asn Leu Ala Asn Tyr Glu Ile His Ala Phe Arg Arg Ile Gly Leu Asn
1745 1750 1755 1760

Ser Ser Ala Cys Tyr Lys Ala Val Glu Ile Ser Thr Leu Ile Arg Arg
1765 1770 1775

Cys Leu Glu Pro Gly Glu Asp Gly Leu Phe Leu Gly Glu Gly Ser Gly
1780 1785 1790

Ser Met Leu Ile Thr Tyr Lys Glu Ile Leu Lys Leu Asn Lys Cys Phe
1795 1800 1805

Tyr Asn Ser Gly Val Ser Ala Asn Ser Arg Ser Gly Gln Arg Glu Leu
1810 1815 1820

Ala Pro Tyr Pro Ser Glu Val Gly Leu Val Glu His Arg Met Gly Val
1825 1830 1835 1840

Gly Asn Ile Val Lys Val Leu Phe Asn Gly Arg Pro Glu Val Thr Trp
1845 1850 1855

Val Gly Ser Val Asp Cys Phe Asn Phe Ile Val Ser Asn Ile Pro Thr
1860 1865 1870

Ser Ser Val Gly Phe Ile His Ser Asp Ile Glu Thr Leu Pro Asp Lys
1875 1880 1885

Asp Thr Ile Glu Lys Leu Glu Glu Leu Ala Ala Ile Leu Ser Met Ala
1890 1895 1900

Leu Leu Leu Gly Lys Ile Gly Ser Ile Leu Val Ile Lys Leu Met Pro
1905 1910 1915 1920

Phe Ser Gly Asp Phe Val Gln Gly Phe Ile Ser Tyr Val Gly Ser His
1925 1930 1935

Tyr Arg Glu Val Asn Leu Val Tyr Pro Arg Tyr Ser Asn Phe Ile Ser
1940 1945 1950

Thr Glu Ser Tyr Leu Val Met Thr Asp Leu Lys Ala Asn Arg Leu Met
1955 1960 1965

Asn Pro Glu Lys Ile Lys Gln Gln Ile Ile Glu Ser Ser Val Arg Thr
1970 1975 1980

Ser Pro Gly Leu Ile Gly His Ile Leu Ser Ile Lys Gln Leu Ser Cys
1985 1990 1995 2000

Ile Gln Ala Ile Val Gly Asp Ala Val Ser Arg Gly Asp Ile Asn Pro
2005 2010 2015

Thr Leu Lys Lys Leu Thr Pro Ile Glu Gln Val Leu Ile Asn Cys Gly
2020 2025 2030

Leu Ala Ile Asn Gly Pro Lys Leu Cys Lys Glu Leu Ile His His Asp
2035 2040 2045

Val Ala Ser Gly Gln Asp Gly Leu Leu Asn Ser Ile Leu Ile Leu Tyr
2050 2055 2060

Arg Glu Leu Ala Arg Phe Lys Asp Asn Gln Arg Ser Gln Gln Gly Met
2065 2070 2075 2080

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Ser Arg Ile Thr Arg Lys Phe Trp Gly His Ile Leu Leu Tyr Ser Gly
2100 2105 2110

Asn Lys Lys Leu Ile Asn Lys Phe Ile Gln Asn Leu Lys Ser Gly Tyr
2115 2120 2125

Leu Ile Leu Asp Leu His Gln Asn Ile Phe Val Lys Asn Leu Ser Lys
2130 2135 2140

Ser Glu Lys Gln Ile Ile Met Thr Gly Gly Leu Lys Arg Glu Trp Val
2145 2150 2155 2160

Phe Lys Val Thr Val Lys Glu Thr Lys Glu Trp Tyr Lys Leu Val Gly
2165 2170 2175

Tyr Ser Ala Leu Ile Lys Asp
2180

(2) INFORMATION FOR SEQ ID NO:13:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 15894 base pairs

(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:

ACCAAACAAA GTTGGGTAAG GATAGTTCAA TCAATGATCA TTTTCTAGTG CACTTAGGAT 60

TCAAGATCCT ATTATCAGGG ACAAGAGCAG GATTAAGGAT ATCCGAGATG GCCACACTTT 120

TAAGGAGCTT AGCATTGTTC AAAAGAAACA AGGACAAACC ACCCATTACA TCAGGATCCG 180

GTGGAGCCAT CAGAGGAATC AAACACATTA TTATAGTACC AATCCCTGGA GATTCCTCAA 240

TTACCACTCG ATCCAGACTT CTGGACCGGT TGGTCAGGTT AATTGGAAAC CCGGATGTGA 300

GCGGGCCCAA ACTAACAGGG GCACTAATAG GTATATTATC CTTATTTGTG GAGTCTCCAG 360

GTCAATTGAT TCAGAGGATC ACCGATGACC CTGACGTTAG CATAAGGCTG TTAGAGGTTG 420

TCCAGAGTGA CCAGTCACAA TCTGGCCTTA CCTTCGCATC AAGAGGTACC AACATGGAGG 480

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GATGGTTCGA GAACAAGGAA ATCTCAGATA TTGAAGTGCA AGACCCTGAG GGATTCAACA 600

TGATTCTGGG TACCATCCTA GCTCAAATTT GGGTCTTGCT CGCAAAGGCG GTTACGGCCC 660

CAGACACGGC AGCTGATTCG GAGCTAAGAA GGTGGATAAA GTACACCCAA CAAAGAAGGG 720

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GAAACAAACC CAGGATTGCT GAAATGATAT GTGACATTGA TACATATATC GTAGAGGCAG 900

GATTAGCCAG TTTTATCCTG ACTATTAAGT TTGGGATAGA AACTATGTAT CCTGCTCTTG 960

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ATGATGTTGC AAAATTGCTC AAAGATATCA ACACAAGCAA GCACAATCTT CCCATTTCAG 14460

GGGGCAATCT CGCCAATTAT GAAATCCATG CTTTCCGCAG AATCGGGTTG AACTCATCTG 14520

CTTGCTACAA AGCTGTTGAG ATATCAACAT TAATTAGGAG ATGCCTTGAG CCAGGGGAGG 14580

ACGGCTTGTT CTTGGGTGAG GGATCGGGTT CTATGTTGAT CACTTATAAG GAGATACTTA 14640

AACTAAACAA GTGCTTCTAT AATAGTGGGG TTTCCGCCAA TTCTAGATCT GGTCAAAGGG 14700

AATTAGCACC CTATCCCTCC GAAGTTGGCC TTGTCGAACA CAGAATGGGA GTAGGTAATA 14760

TTGTCAAAGT GCTCTTTAAC GGGAGGCCCG AAGTCACGTG GGTAGGCAGT GTAGATTGCT 14820

TCAATTTCAT AGTTAGTAAT ATCCCTACCT CTAGTGTGGG GTTTATCCAT TCAGATATAG 14880

AGACCTTGCC TAACAAAGAT ACTATAGAGA AGCTAGAGGA ATTGGCAGCC ATCTTATCGA 14940

TGGCTCTGCT CCTGGGCAAA ATAGGATCAA TACTGGTGAT TAAGCTTATG CCTTTCAGCG 15000

GGGATTTTGT TCAGGGATTT ATAAGTTATG TAGGGTCCCA TTATAGAGAA GTGAACCTTG 15060

TATACCCTAG ATACAGCAAC TTCATATCTA CTGAATCTTA TTTGGTTATG ACAGATCTCA 15120

AGGCTAACCG GCTAATGAAT CCTGAAAAGA TTAAGCAGCA GATAATTGAA TCATCTGTGA 15180

GGACTTCACC TGGACTTATA GGTCACATCC TATCCATTAA GCAACTAAGC TGCATACAAG 15240

CAATTGTGGG AGACGCAGTT AGTAGAGGTG ATATCAATCC TACTCTGAAA AAACTTACAC 15300

CTATAGAGCA GGTGCTGATC AATTGCGGGT TGGCAATTAA CGGACCTAAG CTGTGCAAAG 15360

AATTGATCCA CCATGATGTT GCCTCAGGGC AAGATGGATT GCTTAATTCT ATACTCATCC 15420

TCTACAGGGA GTTGGCAAGA TTCAAAGACA ACCAAAGAAG TCAACAAGGG ATGTTCCACG 15480

CTTACCCCGT ATTGGTAAGT AGCAGGCAAC GAGAACTTAT ATCTAGGATC ACCCGCAAAT 15540

TTTGGGGGCA CATTCTTCTT TACTCCGGGA ACAGAAAGTT GATAAATAAG TTTATCCAGA 15600

ATCTCAAGTC CGGCTATCTG ATACTAGACT TACACCAGAA TATCTTCGTT AAGAATCTAT 15660

CCAAGTCAGA GAAACAGATT ATTATGACGG GGGGTTTGAA ACGTGAGTGG GTTTTTAAGG 15720

TAACAGTCAA GGAGACCAAA GAATGGTATA AGTTAGTCGG ATACAGTGCC CTGATTAAGG 15780

ACTAATTGGT TGAACTCCGG AACCCTAATC CTGCCCTAGG TGGTTAGGCA TTATTTGCAA 15840

TAGATTAAAG AAAACTTTGA AAATACGAAG TTTCTATTCC CAGCTTTGTC TGGT 15894

(2) INFORMATION FOR SEQ ID NO:14:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2183 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

Met Asp Ser Leu Ser Val Asn Gln Ile Leu Tyr Pro Glu Val His Leu
1 5 10 15

Asp Ser Pro Ile Val Thr Asn Lys Ile Val Ala Ile Leu Glu Tyr Ala
20 25 30

Arg Val Pro His Ala Tyr Ser Leu Glu Asp Pro Thr Leu Cys Gln Asn
35 40 45

Ile Lys His Arg Leu Lys Asn Gly Phe Ser Asn Gln Met Ile Ile Asn
50 55 60

Asn Val Glu Val Gly Asn Val Ile Lys Ser Lys Leu Arg Ser Tyr Pro
65 70 75 80

Ala His Ser His Ile Pro Tyr Pro Asn Cys Asn Gln Asp Leu Phe Asn

85 90 95

Ile Glu Asp Lys Glu Ser Thr Arg Lys Ile Arg Glu Leu Leu Lys Lys
100 105 110

Gly Asn Ser Leu Tyr Ser Lys Val Ser Asp Lys Val Phe Gln Cys Leu
115 120 125

Arg Asp Thr Asn Ser Arg Leu Gly Leu Gly Ser Glu Leu Arg Glu Asp
130 135 140

Ile Lys Glu Lys Val Ile Asn Leu Gly Val Tyr Met His Ser Ser Gln
145 150 155 160

Trp Phe Glu Pro Phe Leu Phe Trp Phe Thr Val Lys Thr Glu Met Arg
165 170 175

Ser Val Ile Lys Ser Gln Thr His Thr Cys His Arg Arg Arg His Thr
180 185 190

Pro Val Phe Phe Thr Gly Ser Ser Val Glu Leu Leu Ile Ser Arg Asp
195 200 205

Leu Val Ala Ile Ile Ser Lys Glu Ser Gln His Val Tyr Tyr Leu Thr
210 215 220

Phe Glu Leu Val Leu Met Tyr Cys Asp Val Ile Glu Gly Arg Leu Met
225 230 235 240

Thr Glu Thr Ala Met Thr Ile Asp Ala Arg Tyr Thr Glu Leu Leu Gly
245 250 255

Arg Val Arg Tyr Met Trp Lys Leu Ile Asp Gly Phe Phe Pro Ala Leu
260 265 270

Gly Asn Pro Thr Tyr Gln Ile Val Ala Met Leu Glu Pro Leu Ser Leu
275 280 285

Ala Tyr Leu Gln Leu Arg Asp Ile Thr Val Glu Leu Arg Gly Ala Phe
290 295 300

Leu Asn His Cys Phe Thr Glu Ile His Asp Val Leu Asp Gln Asn Gly
305 310 315 320

Phe Ser Asp Glu Gly Thr Tyr His Glu Leu Ile Glu Ala Leu Asp Tyr
325 330 335

Ile Phe Ile Thr Asp Asp Ile His Leu Thr Gly Glu Ile Phe Ser Phe
340 345 350

Phe Arg Ser Phe Gly His Pro Arg Leu Glu Ala Val Thr Ala Ala Glu
355 360 365

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Asn Val Arg Lys Tyr Met Asn Gln Pro Lys Val Ile Val Tyr Glu Thr
    370                 375                 380

Leu Met Lys Gly His Ala Ile Phe Cys Gly Ile Ile Ile Asn Gly Tyr
385                 390                 395                 400

Arg Asp Arg His Gly Gly Ser Trp Pro Pro Leu Thr Leu Pro Leu His
                405                 410                 415

Ala Ala Asp Thr Ile Arg Asn Ala Gln Ala Ser Gly Glu Gly Leu Thr
            420                 425                 430

His Glu Gln Cys Val Asp Asn Trp Lys Ser Phe Ala Gly Val Lys Phe
        435                 440                 445

Gly Cys Phe Met Pro Leu Ser Leu Asp Ser Asp Leu Thr Met Tyr Leu
    450                 455                 460

Lys Asp Lys Ala Leu Ala Ala Leu Gln Arg Glu Trp Asp Ser Val Tyr
465                 470                 475                 480

Pro Lys Glu Phe Leu Arg Tyr Asp Pro Pro Lys Gly Thr Gly Ser Arg
                485                 490                 495

Arg Leu Val Asp Val Phe Leu Asn Asp Ser Ser Phe Asp Pro Tyr Asp
            500                 505                 510

Val Ile Met Tyr Val Val Ser Gly Ala Tyr Leu His Asp Pro Glu Phe
        515                 520                 525

Asn Leu Ser Tyr Ser Leu Lys Glu Lys Glu Ile Lys Glu Thr Gly Arg
    530                 535                 540

Leu Phe Ala Lys Met Thr Tyr Lys Met Arg Ala Cys Gln Val Ile Ala
545                 550                 555                 560

Glu Asn Leu Ile Ser Asn Gly Ile Gly Lys Tyr Phe Lys Asp Asn Gly
                565                 570                 575

Met Ala Lys Asp Glu His Asp Leu Thr Lys Ala Leu His Thr Leu Ala
            580                 585                 590

Val Ser Gly Val Pro Lys Asp Leu Lys Glu Ser His Arg Gly Gly Pro
        595                 600                 605

Val Leu Lys Thr Tyr Ser Arg Ser Pro Val His Thr Ser Thr Arg Asn
    610                 615                 620

Val Arg Ala Ala Lys Gly Phe Ile Gly Phe Pro Gln Val Ile Arg Gln
625                 630                 635                 640
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Asp Gln Asp Thr Asp His Pro Glu Asn Met Glu Ala Tyr Glu Thr Val
645 650 655

Ser Ala Phe Ile Thr Thr Asp Leu Lys Lys Tyr Cys Leu Asn Trp Arg
660 665 670

Tyr Glu Thr Ile Ser Leu Phe Ala Gln Arg Leu Asn Glu Ile Tyr Gly
675 680 685

Leu Pro Ser Phe Phe Gln Trp Leu His Lys Arg Leu Glu Thr Ser Val
690 695 700

Leu Tyr Val Ser Asp Pro His Cys Pro Pro Asp Leu Asp Ala His Ile
705 710 715 720

Pro Leu Tyr Lys Val Pro Asn Asp Gln Ile Phe Ile Lys Tyr Pro Met
725 730 735

Gly Gly Ile Glu Gly Tyr Cys Gln Lys Leu Trp Thr Ile Ser Thr Ile
740 745 750

Pro Tyr Leu Tyr Leu Ala Ala Tyr Glu Ser Gly Val Arg Ile Ala Ser
755 760 765

Leu Val Gln Gly Asp Asn Gln Thr Ile Ala Val Thr Lys Arg Val Pro
770 775 780

Ser Thr Trp Pro Tyr Asn Leu Lys Lys Arg Glu Ala Ala Arg Val Thr
785 790 795 800

Arg Asp Tyr Phe Val Ile Leu Arg Gln Arg Leu His Asp Ile Gly His
805 810 815

His Leu Lys Ala Asn Glu Thr Ile Val Ser Ser His Phe Phe Val Tyr
820 825 830

Ser Lys Gly Ile Tyr Tyr Asp Gly Leu Leu Val Ser Gln Ser Leu Lys
835 840 845

Ser Ile Ala Arg Cys Val Phe Trp Ser Glu Thr Ile Val Asp Glu Thr
850 855 860

Arg Ala Ala Cys Ser Asn Ile Ala Thr Thr Met Ala Lys Ser Ile Glu
865 870 875 880

Arg Gly Tyr Asp Arg Tyr Leu Ala Tyr Ser Leu Asn Val Leu Lys Val
885 890 895

Ile Gln Gln Ile Leu Ile Ser Leu Gly Phe Thr Ile Asn Ser Thr Met
900 905 910

Thr Arg Asp Val Val Ile Pro Leu Leu Thr Asn Asn Asp Leu Leu Ile

915 920 925

Arg Met Ala Leu Leu Pro Ala Pro Ile Gly Gly Met Asn Tyr Leu Asn
930 935 940

Met Ser Arg Leu Phe Val Arg Asn Ile Gly Asp Pro Val Thr Ser Ser
945 950 955 960

Ile Ala Asp Leu Lys Arg Met Ile Leu Ala Ser Leu Met Pro Glu Glu
965 970 975

Thr Leu His Gln Val Met Thr Gln Gln Pro Gly Asp Ser Ser Phe Leu
980 985 990

Asp Trp Ala Ser Asp Pro Tyr Ser Ala Asn Leu Val Cys Val Gln Ser
995 1000 1005

Ile Thr Arg Leu Leu Lys Asn Ile Thr Ala Arg Phe Val Leu Ile His
1010 1015 1020

Ser Pro Asn Pro Met Leu Lys Gly Leu Phe His Asp Asp Ser Lys Glu
1025 1030 1035 1040

Glu Asp Glu Gly Leu Ala Ala Phe Leu Met Asp Arg His Ile Ile Val
1045 1050 1055

Pro Arg Ala Ala His Glu Ile Leu Asp His Ser Val Thr Gly Ala Arg
1060 1065 1070

Glu Ser Ile Ala Gly Met Leu Asp Thr Thr Lys Gly Leu Ile Arg Ala
1075 1080 1085

Ser Met Arg Lys Gly Gly Leu Thr Ser Arg Val Ile Thr Arg Leu Ser
1090 1095 1100

Asn Tyr Asp Tyr Glu Gln Phe Arg Ala Gly Met Val Leu Leu Thr Gly
1105 1110 1115 1120

Arg Lys Arg Asn Val Leu Ile Asp Lys Glu Ser Cys Ser Val Gln Leu
1125 1130 1135

Ala Arg Ala Leu Arg Ser His Met Trp Ala Arg Leu Ala Arg Gly Arg
1140 1145 1150

Pro Ile Tyr Gly Leu Glu Val Pro Asp Val Leu Glu Ser Met Arg Gly
1155 1160 1165

His Leu Ile Arg Arg His Glu Thr Cys Val Ile Cys Glu Cys Gly Ser
1170 1175 1180

Val Asn Tyr Gly Trp Phe Phe Val Pro Ser Gly Cys Gln Leu Asp Asp
1185 1190 1195 1200

Ile Asp Lys Glu Thr Ser Ser Leu Arg Val Pro Tyr Ile Gly Ser Thr
1205 1210 1215

Thr Asp Glu Arg Thr Asp Met Lys Leu Ala Phe Val Arg Ala Pro Ser
1220 1225 1230

Arg Ser Leu Arg Ser Ala Val Arg Ile Ala Thr Val Tyr Ser Trp Ala
1235 1240 1245

Tyr Gly Asp Asp Asp Ser Ser Trp Asn Glu Ala Trp Leu Leu Ala Arg
1250 1255 1260

Gln Arg Ala Asn Val Ser Leu Glu Glu Leu Arg Val Ile Thr Pro Ile
1265 1270 1275 1280

Ser Thr Ser Thr Asn Leu Ala His Arg Leu Arg Asp Arg Ser Thr Gln
1285 1290 1295

Val Lys Tyr Ser Gly Thr Ser Leu Val Arg Val Ala Arg Tyr Thr Thr
1300 1305 1310

Ile Ser Asn Asp Asn Leu Ser Phe Val Ile Ser Asp Lys Lys Val Asp
1315 1320 1325

Thr Asn Phe Ile Tyr Gln Gln Gly Met Leu Leu Gly Leu Gly Val Leu
1330 1335 1340

Glu Thr Leu Phe Arg Leu Glu Lys Asp Thr Gly Ser Ser Asn Thr Val
1345 1350 1355 1360

Leu His Leu His Val Glu Thr Asp Cys Cys Val Ile Pro Met Ile Asp
1365 1370 1375

His Pro Arg Ile Pro Ser Ser Arg Lys Leu Glu Leu Arg Ala Glu Leu
1380 1385 1390

Cys Thr Asn Pro Leu Ile Tyr Asp Asn Ala Pro Leu Ile Asp Arg Asp
1395 1400 1405

Thr Thr Arg Leu Tyr Thr Gln Ser His Arg Arg His Leu Val Glu Phe
1410 1415 1420

Val Thr Trp Ser Thr Pro Gln Leu Tyr His Ile Leu Ala Lys Ser Thr
1425 1430 1435 1440

Ala Leu Ser Met Ile Asp Leu Val Thr Lys Phe Glu Lys Asp His Met
1445 1450 1455

Asn Glu Ile Ser Ala Leu Ile Gly Asp Asp Asp Ile Asn Ser Phe Ile
1460 1465 1470

Thr Glu Phe Leu Leu Ile Glu Pro Arg Leu Phe Thr Ile Tyr Leu Gly
1475 1480 1485

Gln Cys Ala Ala Ile Asn Trp Ala Phe Asp Val His Tyr His Arg Pro
1490 1495 1500

Ser Gly Lys Tyr Gln Met Gly Glu Leu Leu Ser Ser Phe Leu Ser Arg
1505 1510 1515 1520

Met Ser Lys Gly Val Phe Lys Val Leu Val Asn Ala Leu Ser His Pro
1525 1530 1535

Lys Ile Tyr Lys Lys Phe Trp His Cys Gly Ile Ile Glu Pro Ile His
1540 1545 1550

Gly Pro Ser Leu Asp Ala Gln Asn Leu His Thr Thr Val Cys Asn Met
1555 1560 1565

Val Tyr Thr Cys Tyr Met Thr Tyr Leu Asp Leu Leu Leu Asn Glu Glu
1570 1575 1580

Leu Glu Glu Phe Thr Phe Leu Leu Cys Glu Ser Asp Glu Asp Val Val
1585 1590 1595 1600

Pro Asp Arg Phe Asp Asn Ile Gln Ala Lys His Leu Cys Val Leu Ala
1605 1610 1615

Asp Leu Tyr Cys Gln Pro Gly Thr Cys Pro Pro Ile Arg Gly Leu Arg
1620 1625 1630

Pro Val Glu Lys Cys Ala Val Leu Thr Asp His Ile Lys Ala Glu Ala
1635 1640 1645

Arg Leu Ser Pro Ala Gly Ser Ser Trp Asn Ile Asn Pro Ile Ile Val
1650 1655 1660

Asp His Tyr Ser Cys Ser Leu Thr Tyr Leu Arg Arg Gly Ser Ile Lys
1665 1670 1675 1680

Gln Ile Arg Leu Arg Val Asp Pro Gly Phe Ile Phe Asp Ala Leu Ala
1685 1690 1695

Glu Val Asn Val Ser Gln Pro Lys Ile Gly Ser Asn Asn Ile Ser Asn
1700 1705 1710

Met Ser Ile Lys Ala Phe Arg Pro Pro His Asp Asp Val Ala Lys Leu
1715 1720 1725

Leu Lys Asp Ile Asn Thr Ser Lys His Asn Leu Pro Ile Ser Gly Gly
1730 1735 1740

Asn Leu Ala Asn Tyr Glu Ile His Ala Phe Arg Arg Ile Gly Leu Asn

1745 1750 1755 1760

Ser Ser Ala Cys Tyr Lys Ala Val Glu Ile Ser Thr Leu Ile Arg Arg
1765 1770 1775

Cys Leu Glu Pro Gly Glu Asp Gly Leu Phe Leu Gly Glu Gly Ser Gly
1780 1785 1790

Ser Met Leu Ile Thr Tyr Lys Glu Ile Leu Lys Leu Asn Lys Cys Phe
1795 1800 1805

Tyr Asn Ser Gly Val Ser Ala Asn Ser Arg Ser Gly Gln Arg Glu Leu
1810 1815 1820

Ala Pro Tyr Pro Ser Glu Val Gly Leu Val Glu His Arg Met Gly Val
1825 1830 1835 1840

Gly Asn Ile Val Lys Val Leu Phe Asn Gly Arg Pro Glu Val Thr Trp
1845 1850 1855

Val Gly Ser Val Asp Cys Phe Asn Phe Ile Val Ser Asn Ile Pro Thr
1860 1865 1870

Ser Ser Val Gly Phe Ile His Ser Asp Ile Glu Thr Leu Pro Asn Lys
1875 1880 1885

Asp Thr Ile Glu Lys Leu Glu Glu Leu Ala Ala Ile Leu Ser Met Ala
1890 1895 1900

Leu Leu Leu Gly Lys Ile Gly Ser Ile Leu Val Ile Lys Leu Met Pro
1905 1910 1915 1920

Phe Ser Gly Asp Phe Val Gln Gly Phe Ile Ser Tyr Val Gly Ser His
1925 1930 1935

Tyr Arg Glu Val Asn Leu Val Tyr Pro Arg Tyr Ser Asn Phe Ile Ser
1940 1945 1950

Thr Glu Ser Tyr Leu Val Met Thr Asp Leu Lys Ala Asn Arg Leu Met
1955 1960 1965

Asn Pro Glu Lys Ile Lys Gln Gln Ile Ile Glu Ser Ser Val Arg Thr
1970 1975 1980

Ser Pro Gly Leu Ile Gly His Ile Leu Ser Ile Lys Gln Leu Ser Cys
1985 1990 1995 2000

Ile Gln Ala Ile Val Gly Asp Ala Val Ser Arg Gly Asp Ile Asn Pro
2005 2010 2015

Thr Leu Lys Lys Leu Thr Pro Ile Glu Gln Val Leu Ile Asn Cys Gly
2020 2025 2030

Leu Ala Ile Asn Gly Pro Lys Leu Cys Lys Glu Leu Ile His His Asp
2035 2040 2045

Val Ala Ser Gly Gln Asp Gly Leu Leu Asn Ser Ile Leu Ile Leu Tyr
2050 2055 2060

Arg Glu Leu Ala Arg Phe Lys Asp Asn Gln Arg Ser Gln Gln Gly Met
2065 2070 2075 2080

Phe His Ala Tyr Pro Val Leu Val Ser Ser Arg Gln Arg Glu Leu Ile
2085 2090 2095

Ser Arg Ile Thr Arg Lys Phe Trp Gly His Ile Leu Leu Tyr Ser Gly
2100 2105 2110

Asn Arg Lys Leu Ile Asn Lys Phe Ile Gln Asn Leu Lys Ser Gly Tyr
2115 2120 2125

Leu Ile Leu Asp Leu His Gln Asn Ile Phe Val Lys Asn Leu Ser Lys
2130 2135 2140

Ser Glu Lys Gln Ile Ile Met Thr Gly Gly Leu Lys Arg Glu Trp Val
2145 2150 2155 2160

Phe Lys Val Thr Val Lys Glu Thr Lys Glu Trp Tyr Lys Leu Val Gly
2165 2170 2175

Tyr Ser Ala Leu Ile Lys Asp
2180

(2) INFORMATION FOR SEQ ID NO:15:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 15894 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

ACCAAACAAA GTTGGGTAAG GATAGTTCAA TCAATGATCA TCTTCTAGTG CACTTAGGAT 60

TCAAGATCCT ATTATCAGGG ACAAGAGCAG GATTAGGGAT ATCCGAGATG GCCACACTTT 120

TAAGGAGCTT AGCATTGTTC AAAAGAAACA AGGACAAACC ACCCATTACA TCAGGATCCG 180

GTGGAGCCAT CAGAGGAATC AAACACATTA TTATAGTACC AATCCCTGGA GATTCCTCAA 240

TTACCACTCG ATCCAGACTT CTGGACCGGT TGGTCAGGTT AATTGGAAAC CCGGATGTGA 300

GCGGGCCCAA ACTAACAGGG GCACTAATAG GTATATTATC CTTATTTGTG GAGTCTCCAG 360

GTCAATTGAT TCAGAGGATC ACCGATGACC CTGACGTTAG CATAAGGCTG TTAGAGGTTG 420

TCCAGAGTGA CCAGTCACAA TCTGGCCTTA CCTTCGCATC AAGAGGTACC AACATGGAGG 480

ATGAGGCGGA CAAATACTTT TCACATGATG ATCCAATTAG TAGTGATCAA TCCAGGTTCG 540

GATGGTTCGA GAACAAGGAA ATCTCAGATA TTGAAGTGCA AGACCCTGAG GGATTCAACA 600

TGATTCTGGG TACCATCCTA GCCCAAATTT GGGTCTTGCT CGCAAAGGCG GTTACGGCCC 660

CAGACACGGC AGCTGATTCG GAGCTAAGAA GGTGGATAAA GTACACCCAA CAAAGAAGGG 720

TAGTTGGTGA ATTTAGATTG GAGAGAAAAT GGTTGGATGT GGTGAGGAAC AGGATTGCCG 780

AGGACCTCTC CTTACGCCGA TTCATGGTCG CTCTAATCCT GGATATCAAG AGAACACCCG 840

GAAACAAACC CAGGATTGCT GAAATGATAT GTGACATTGA TACATATATC GTAGAGGCAG 900

GATTAGCCAG TTTTATCCTG ACTATTAAGT TTGGGATAGA AACTATGTAT CCTGCTCTTG 960

GACTGCATGA ATTTGCTGGT GAGTTATCCA CACTTGAGTC CTTGATGAAC CTTTACCAGC 1020

AAATGGGGGA AACTGCACCC TACATGGTAA TCCTGGAGAA CTCAATTCAG AACAAGTTCA 1080

GTGCAGGATC ATACCCTCTG CTCTGGAGCT ATGCCATGGG AGTAGGAGTG GAACTTGAAA 1140

ACTCCATGGG AGGTTTGAAC TTTGGCCGAT CTTACTTTGA TCCAGCATAT TTTAGATTAG 1200

GGCAAGAGAT GGTAAGGAGG TCAGCTGGAA AGGTCAGTTC CACATTGGCA TCTGAACTCG 1260

GTATCACTGC CGAGGATGCA AGGCTTGTTT CAGAGATTGC AATGCATACT ACTGAGGACA 1320

AGATCAGTAG AGCGGTTGGA CCCAGACAAG CCCAAGTATC ATTTCTACAC GGTGATCAAA 1380

GTGAGAATGA GCTACCGAGA TTGGGGGGCA AGGAAGATAG GAGGGTCAAA CAGAGTCGAG 1440

GAGAAGCCAG GGAGAGCTAC AGAGAAACCG GGCCCAGCAG AGCAAGTGAT GCGAGAGCTG 1500

CCCATCTTCC AACCGGCACA CCCCTAGACA TTGACACTGC ATCGGAGTCC AGCCAAGATC 1560

CGCAGGACAG TCGAAGGTCA GCTGACGCCC TGCTTAGGCT GCAAGCCATG GCAGGAATCT 1620

CGGAAGAACA AGGCTCAGAC ACGGACACCC CTATAGTGTA CAATGACAGA AATCTTCTAG 1680

ACTAGGTGCG AGAGGCCGAG GACCAGAACA ACATCCGCCT ACCCTCCATC ATTGTTATAA 1740

AAAACTTAGG AACCAGGTCC ACACAGCCGC CAGCCCATCA ACCATCCACT CCCACGATTG 1800

GAGCCGATGG CAGAAGAGCA GGCACGCCAT GTCAAAAACG GACTGGAATG CATCCGGGCT 1860

CTCAAGGCCG AGCCCATCGG CTCACTGGCC ATCGAGGAAG CTATGGCAGC ATGGTCAGAA 1920

ATATCAGACA ACCCAGGACA GGAGCGAGCC ACCTGCAGGG AAGAGAAGGC AGGCAGTTCG 1980

GGTCTCAGCA AACCATGCCT CTCAGCAATT GGATCAACTG AAGGCGGTGC ACCTCGCATC 2040

CGCGGTCAGG GACCTGGAGA GAGCGATGAC GACGCTGAAA CTTTGGGAAT CCCCCCAAGA 2100

AATCTCCAGG CATCAAGCAC TGGGTTACAG TGTTATTATG TTTATGATCA CAGCGGTGAA 2160

GCGGTTAAGG GAATCCAAGA TGCTGACTCT ATCATGGTTC AATCAGGCCT TGATGGTGAT 2220

AGCACCCTAT CAGGAGGAGA CAATGAATCT GAAAACAGCG ATGTGGATAT TGGCGAACCT 2280

GATACCGAGG GATATGCTAT CACTGACCGG GGATCTGCTC CCATCTCTAT GGGGTTCAGG 2340

GCTTCTGATG TTGAAACTGC AGAAGGAGGG GAGATCCACG AGCTCCTGAG ACTCCAATCC 2400

AGAGGCAACA ACTTTCCGAA GCTTGGGAAA ACTCTCAATG TTCCTCCGCC CCCGGACCCC 2460

GGTAGGGCCA GCACTTCCGG GACACCCATT AAAAAGGGCA CAGACGCGAG ATTAGCCTCA 2520

TTTGGAACGG AGATCGCGTC TTTATTGACA GGTGGTGCAA CCCAATGTGC TCGAAAGTCA 2580

CCCTCGGAAC CATCAGGGCC AGGTGCACCT GCGGGGAATG TCCCCGAGTA TGTGAGCAAT 2640

GCCGCACTGA TACAGGAGTG GACACCCGAA TCTGGTACCA CAATCTCCCC GAGATCCCAG 2700

AATAATGAAG AAGGGGGAGA CTATTATGAT GATGAGCTGT TCTCTGATGT CCAAGATATT 2760

AAAACAGCCT TGGCCAAAAT ACACGAGGAT AATCAGAAGA TAATCTCCAA GCTAGAATCA 2820

CTGCTGTTAT TGAAGGGAGA AGTTGAGTCA ATTAAGAAGC AGATCAACAG GCAAAATATC 2880

AGCATATCCA CCCTGGAAGG ACACCTCTCA AGCATCATGA TCGCCATTCC TGGACTTGGG 2940

AAGGATCCCA ACGACCCCAC TGCAGATGTC GAAATCAATC CCGACTTGAA ACCCATCATA 3000

GGCAGAGATT CAGGCCGAGC ACTGGCCGAA GTTCTCAAGA AACCCGTTGC CAGCCGACAA 3060

CTCCAAGGAA TGACAAATGG ACGGACCAGT TCCAGAGGAC AGCTGCTGAA GGAATTTCAG 3120

CCAAAGCCGA TCGGGAAAAA GATGAGCTCA GCCGTCGGGT TTGTTCCTGA CACCGGCCCT 3180

GCATCACGCA GTGTAATCCG CTCCATTATA AAATCCAGCC GGCTAGAGGA GGATCGGAAG 3240

CGTTACCTGA TGACTCTCCT TGATGATATC AAAGGAGCCA ATGATCTTGC CAAGTTCCAC 3300

CAGATGCTGA TGAAGATAAT AATGAAGTAG CTACAGCTCA ACTTACCTGC CAACCCCATG 3360

CCAGTCGACC CAACTAGTAC AACCTAAATC CATTATAAAA AACTTAGGAG CAAAGTGATT 3420

GCCTCCCAAG TTCCACAATG ACAGAGATCT ACGACTTCGA CAAGTCGGCA TGGGACATCA 3480

AAGGGTCGAT CGCTCCGATA CAACCGACCA CCTACAGTGA TGGCAGGCTG GTGCCCCAGG 3540

TCAGAGTCAT AGATCCTGGT CTAGGCGACA GGAAGGATGA ATGCTTTATG TACATGTCTC 3600

TGCTGGGGGT TGTTGAGGAC AGCGATCCCC TAGGGCCTCC AATCGGGCGA GCATTTGGGT 3660

CCCTGCCCTT AGGTGTTGGC AGATCCACAG CAAAGCCCGA AAAACTCCTC AAAGAGGCCA 3720

CTGAGCTTGA CATAGTTGTT AGACGTACAG CAGGGCTCAA TGAAAAACTG GTGTTCTACA 3780

ACAACACCCC ACTAACTCTC CTCACACCTT GGAGAAAGGT CCTAACAACA GGGAGTGTCT 3840

TCAACGCAAA CCAAGTGTGC AATGCGGTTA ATCTGATACC GCTCGATACC CCGCAGAGGT 3900

TCCGTGTTGT TTATATGAGC ATCACCCGTC TTTCGGATAA CGGGTATTAC ACCGTTCCTA 3960

GAAGAATGCT GGAATTCAGA TCGGTCAATG CAGTGGCCTT CAACCTGCTG GTGACCCTTA 4020

GGATTGACAA GGCGATAGGC CCTGGGAAGA TCATCGACAA TACAGAGCAA CTTCCTGAGG 4080

CAACATTTAT GGTCCACATC GGGAACTTCA GGAGAAAGAA GAGTGAAGTC TACTCTGCCG 4140

ATTATTGCAA AATGAAAATC GAAAAGATGG GCCTGGTTTT TGCACTTGGT GGGATAGGGG 4200

GCACCAGTCT TCACATTAGA AGCACAGGCA AAATGAGCAA GACTCTCCAT GCACAACTCG 4260

GGTTCAAGAA GACCTTATGT TACCCGCTGA TGGATATCAA TGAAGACCTT AATCGATTAC 4320

TCTGGAGGAG CAGATGCAAG ATAGTAAGAA TCCAGGCAGT TTTGCAGCCA TCAGTTCCTC 4380

AAGAATTCCG CATTTACGAC GACGTGATCA TAAATGATGA CCAAGGACTA TTCAAAGTTC 4440

TGTAGACCGT AGTGCCCAGC AATGCCCGAA AACGACCCCC CTCACAATGA CAGCCAGAAG 4500

GCCCGGACAA AAAAGCCCCC TCCGAAAGAC TCCACTGACC AAGCGAGAGG CCAGCCAGCA 4560

GCCGACGGCA AGCACGAACA CCAGGCGGCC CCAGCACAGA ACAGCCCTGA TACAAGGCCA 4620

CCACCAGCCA CCCCAATCTG CATCCTCCTC GTGGGACCCC CGAGGACCAA CCCCCAAGGC 4680

TGCCCCCGAT CCAAACCACC AACCGCATCC CCACCACCCC CGGGAAAGAA ACCCCCAGCA 4740

ATTGGAAGGC CCCTCCCCCT CTTCCTCAAC ACAAGAACTC CACAACCGAA CCGCACAAGC 4800

GACCGAGGTG ACCCAACCGC AGGCATCCGA CTCCCTAGAC AGATCCTCTC TCCCCGGCAA 4860

ACTAAACAAA ACTTAGGGCC AAGGAACATA CACACCCAAC AGAACCCAGA CCCCGGCCCA 4920

CGGCGCCGCG CCCCCAACCC CCGACAACCA GAGGGAGCCC CCAACCAATC CCGCCGGCTC 4980

CCCCGGTGCC CACAGGCAGG GACACCAACC CCCGAACAGA CCCAGCACCT AACCATCGAC 5040

AATCCAAGAC GGGGGGGCCC CCCCAAAAAA AGGCCCCCAG GGGCCGACAG CCAGCACCGC 5100

GAGGAAGCCC ACCCACCCCA CACACGACCA CGGCAACCAA ACCAGAACCC AGACCACCCT 5160

GGGCCACCAG CTCCCAGACT CGGCCATCAC CCCGCAGAAA GGAAAGGCCA CAACCCGCGC 5220

ACCCCAGCCC CGATCCGGCG GGGAGCCACC CAACCCGAAC CAGCACCCAA GAGCGATCCC 5280

CGAAGGACCC CCGAACCGCA AAGGACATCA GTATCCCACA GCCTCTCCAA GTCCCCCGGT 5340

CTCCTCCTCT TCTCGAAGGG ACCAAAAGAT CAATCCACCA CACCCGACGA CACTCAACTC 5400

CCCACCCCTA AAGGAGACAC CGGGAATCCC AGAATCAAGA CTCATCCAAT GTCCATCATG 5460

GGTCTCAAGG TGAACGTCTC TGCCATATTC ATGGCAGTAC TGTTAACTCT CCAAACACCC 5520

ACCGGTCAAA TCCATTGGGG CAATCTCTCT AAGATAGGGG TGGTAGGAAT AGGAAGTGCA 5580

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CACAACAACC GGGGGACTCT TCATTCCTAG ACTGGGCTAG CGACCCTTAC TCAGCAAATC 12240
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TATATTAAAG AAAACTTTGA AAATACGAAG TTTCTATTCC CAGCTTTGTC TGGT 15894

(2) INFORMATION FOR SEQ ID NO:16:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2183 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:

Met Asp Ser Leu Ser Val Asn Gln Ile Leu Tyr Pro Glu Val His Leu
1 5 10 15

Asp Ser Pro Ile Val Thr Asn Lys Ile Val Ala Ile Leu Glu Tyr Ala
20 25 30

Arg Val Pro His Ala Tyr Ser Leu Glu Asp Pro Thr Leu Cys Gln Asn
35 40 45

Ile Lys His Arg Leu Lys Asn Gly Phe Ser Asn Gln Met Ile Ile Asn
50 55 60

Asn Val Glu Val Gly Asn Val Ile Lys Ser Lys Leu Arg Ser Tyr Pro
65 70 75 80

Ala His Ser His Ile Pro Tyr Pro Asn Cys Asn Gln Asp Leu Phe Asn
85 90 95

Ile Glu Asp Lys Glu Ser Thr Arg Lys Ile Arg Glu Leu Leu Lys Lys
100 105 110

Gly Asn Ser Leu Tyr Ser Lys Val Ser Asp Lys Val Phe Gln Cys Leu
115 120 125

Arg Asp Thr Asn Ser Arg Leu Gly Leu Gly Ser Glu Leu Arg Glu Asp
130 135 140

Ile Lys Glu Lys Val Ile Asn Leu Gly Val Tyr Met His Ser Ser Gln
145 150 155 160

Trp Phe Glu Pro Phe Leu Phe Trp Phe Thr Val Lys Thr Glu Met Arg
165 170 175

Ser Val Ile Lys Ser Gln Thr His Thr Cys His Arg Arg Arg His Thr
180 185 190

Pro Val Phe Phe Thr Gly Ser Ser Val Glu Leu Leu Ile Ser Arg Asp
195 200 205

Leu Val Ala Ile Ile Ser Lys Glu Ser Gln His Val Tyr Tyr Leu Thr
210 215 220

Phe Glu Leu Val Leu Met Tyr Cys Asp Val Ile Glu Gly Arg Leu Met
225 230 235 240

Thr Glu Thr Ala Met Thr Ile Asp Ala Arg Tyr Thr Glu Leu Leu Gly
245 250 255

Arg Val Arg Tyr Met Trp Lys Leu Ile Asp Gly Phe Phe Pro Ala Leu
260 265 270

Gly Asn Pro Thr Tyr Gln Ile Val Ala Met Leu Glu Pro Leu Ser Leu
275 280 285

Ala Tyr Leu Gln Leu Arg Asp Ile Thr Val Glu Leu Arg Gly Ala Phe
290 295 300

Leu Asn His Cys Phe Thr Glu Ile His Asp Val Leu Asp Gln Asn Gly
305 310 315 320

Phe Ser Asp Glu Gly Thr Tyr His Glu Leu Ile Glu Ala Leu Asp Tyr
325 330 335

Ile Phe Ile Thr Asp Asp Ile His Leu Thr Gly Glu Ile Phe Ser Phe
340 345 350

Phe Arg Ser Phe Gly His Pro Arg Leu Glu Ala Val Thr Ala Ala Glu
355 360 365

Asn Val Arg Lys Tyr Met Asn Gln Pro Lys Val Ile Val Tyr Glu Thr
370 375 380

Leu Met Lys Gly His Ala Ile Phe Cys Gly Ile Ile Ile Asn Gly Tyr
385 390 395 400

Arg Asp Arg His Gly Gly Ser Trp Pro Pro Leu Thr Leu Pro Leu His
405 410 415

Ala Ala Asp Thr Ile Arg Asn Ala Gln Ala Ser Gly Glu Gly Leu Thr
420 425 430

His Glu Gln Cys Val Asp Asn Trp Lys Ser Phe Ala Gly Val Lys Phe
435 440 445

Gly Cys Phe Met Pro Leu Ser Leu Asp Ser Asp Leu Thr Met Tyr Leu

450 455 460

Lys Asp Lys Ala Leu Ala Ala Leu Gln Arg Glu Trp Asp Ser Val Tyr
465 470 475 480

Pro Lys Glu Phe Leu Arg Tyr Asp Pro Pro Lys Gly Thr Gly Ser Arg
485 490 495

Arg Leu Val Asp Val Phe Leu Asn Asp Ser Ser Phe Asp Pro Tyr Asp
500 505 510

Val Ile Met Tyr Val Val Ser Gly Ala Tyr Leu His Asp Pro Glu Phe
515 520 525

Asn Leu Ser Tyr Ser Leu Lys Glu Lys Glu Ile Lys Glu Thr Gly Arg
530 535 540

Leu Phe Ala Lys Met Thr Tyr Lys Met Arg Ala Cys Gln Val Ile Ala
545 550 555 560

Glu Asn Leu Ile Ser Asn Gly Ile Gly Lys Tyr Phe Lys Asp Asn Gly
565 570 575

Met Ala Lys Asp Glu His Asp Leu Thr Lys Ala Leu His Thr Leu Ala
580 585 590

Val Ser Gly Val Pro Lys Asp Leu Lys Glu Ser His Arg Gly Gly Pro
595 600 605

Val Leu Lys Thr Tyr Ser Arg Ser Pro Val His Thr Ser Thr Arg Asn
610 615 620

Val Arg Ala Ala Lys Gly Phe Ile Gly Phe Pro Gln Val Ile Arg Gln
625 630 635 640

Asp Gln Asp Thr Asp His Pro Glu Asn Met Glu Ala Tyr Glu Thr Val
645 650 655

Ser Ala Phe Ile Thr Thr Asp Leu Lys Lys Tyr Cys Leu Asn Trp Arg
660 665 670

Tyr Glu Thr Ile Ser Leu Phe Ala Gln Arg Leu Asn Glu Ile Tyr Gly
675 680 685

Leu Pro Ser Phe Phe Gln Trp Leu His Lys Arg Leu Glu Thr Ser Val
690 695 700

Leu Tyr Val Ser Asp Pro His Cys Pro Pro Asp Leu Asp Ala His Ile
705 710 715 720

Pro Leu Tyr Lys Val Pro Asn Asp Gln Ile Phe Ile Lys Tyr Pro Met
725 730 735

Gly Gly Ile Glu Gly Tyr Cys Gln Lys Leu Trp Thr Ile Ser Thr Ile
740 745 750

Pro Tyr Leu Tyr Leu Ala Ala Tyr Glu Ser Gly Val Arg Ile Ala Ser
755 760 765

Leu Val Gln Gly Asp Asn Gln Thr Ile Ala Val Thr Lys Arg Val Pro
770 775 780

Ser Thr Trp Pro Tyr Asn Leu Lys Lys Arg Glu Ala Ala Arg Val Thr
785 790 795 800

Arg Asp Tyr Phe Val Ile Leu Arg Gln Arg Leu His Asp Ile Gly His
805 810 815

His Leu Lys Ala Asn Glu Thr Ile Val Ser Ser His Phe Phe Val Tyr
820 825 830

Ser Lys Gly Ile Tyr Tyr Asp Gly Leu Leu Val Ser Gln Ser Leu Lys
835 840 845

Ser Ile Ala Arg Cys Val Phe Trp Ser Glu Thr Ile Val Asp Glu Thr
850 855 860

Arg Ala Ala Cys Ser Asn Ile Ala Thr Thr Met Ala Lys Ser Ile Glu
865 870 875 880

Arg Gly Tyr Asp Arg Tyr Leu Ala Tyr Ser Leu Asn Val Leu Lys Val
885 890 895

Ile Gln Gln Ile Leu Ile Ser Leu Gly Phe Thr Ile Asn Ser Thr Met
900 905 910

Thr Arg Asp Val Val Ile Pro Leu Leu Thr Asn Asn Asp Leu Leu Ile
915 920 925

Arg Met Ala Leu Leu Pro Ala Pro Ile Gly Gly Met Asn Tyr Leu Asn
930 935 940

Met Ser Arg Leu Phe Val Arg Asn Ile Gly Asp Pro Val Thr Ser Ser
945 950 955 960

Ile Ala Asp Leu Lys Arg Met Ile Leu Ala Ser Leu Met Pro Glu Glu
965 970 975

Thr Leu His Gln Val Met Thr Gln Gln Pro Gly Asp Ser Ser Phe Leu
980 985 990

Asp Trp Ala Ser Asp Pro Tyr Ser Ala Asn Leu Val Cys Val Gln Ser
995 1000 1005

Ile Thr Arg Leu Leu Lys Asn Ile Thr Ala Arg Phe Val Leu Ile His
1010 1015 1020

Ser Pro Asn Pro Met Leu Lys Gly Leu Phe His Asp Asp Ser Lys Glu
1025 1030 1035 1040

Glu Asp Glu Gly Leu Ala Ala Phe Leu Met Asp Arg His Ile Ile Val
1045 1050 1055

Pro Arg Ala Ala His Glu Ile Leu Asp His Ser Val Thr Gly Ala Arg
1060 1065 1070

Glu Ser Ile Ala Gly Met Leu Asp Thr Thr Lys Gly Leu Ile Arg Ala
1075 1080 1085

Ser Met Arg Lys Gly Gly Leu Thr Ser Arg Val Ile Thr Arg Leu Ser
1090 1095 1100

Asn Tyr Asp Tyr Glu Gln Phe Arg Ala Gly Met Val Leu Leu Thr Gly
1105 1110 1115 1120

Arg Lys Arg Asn Val Leu Ile Asp Lys Glu Ser Cys Ser Val Gln Leu
1125 1130 1135

Ala Arg Ala Leu Arg Ser His Met Trp Ala Arg Leu Ala Arg Gly Arg
1140 1145 1150

Pro Ile Tyr Gly Leu Glu Val Pro Asp Val Leu Glu Ser Met Arg Gly
1155 1160 1165

His Leu Ile Arg Arg His Glu Thr Cys Val Ile Cys Glu Cys Gly Ser
1170 1175 1180

Val Asn Tyr Gly Trp Phe Phe Val Pro Ser Gly Cys Gln Leu Asp Asp
1185 1190 1195 1200

Ile Asp Lys Glu Thr Ser Ser Leu Arg Val Pro Tyr Ile Gly Ser Thr
1205 1210 1215

Thr Asp Glu Arg Thr Asp Met Lys Leu Ala Phe Val Arg Ala Pro Ser
1220 1225 1230

Arg Ser Leu Arg Ser Ala Val Arg Ile Ala Thr Val Tyr Ser Trp Ala
1235 1240 1245

Tyr Gly Asp Asp Asp Ser Ser Trp Asn Glu Ala Trp Leu Leu Ala Arg
1250 1255 1260

Gln Arg Ala Asn Val Ser Leu Glu Glu Leu Arg Val Ile Thr Pro Ile
1265 1270 1275 1280

Ser Thr Ser Thr Asn Leu Ala His Arg Leu Arg Asp Arg Ser Thr Gln

1285 1290 1295

Val Lys Tyr Ser Gly Thr Ser Leu Val Arg Val Ala Arg Tyr Thr Thr
1300 1305 1310

Ile Ser Asn Asp Asn Leu Ser Phe Val Ile Ser Asp Lys Lys Val Asp
1315 1320 1325

Thr Asn Phe Ile Tyr Gln Gln Gly Met Leu Leu Gly Leu Gly Val Leu
1330 1335 1340

Glu Thr Leu Phe Arg Leu Glu Lys Asp Thr Gly Ser Ser Asn Thr Val
1345 1350 1355 1360

Leu His Leu His Val Glu Thr Asp Cys Cys Val Ile Pro Met Ile Asp
1365 1370 1375

His Pro Arg Ile Pro Ser Ser Arg Lys Leu Glu Leu Arg Ala Glu Leu
1380 1385 1390

Cys Thr Asn Pro Leu Ile Tyr Asp Asn Ala Pro Leu Ile Asp Arg Asp
1395 1400 1405

Thr Thr Arg Leu Tyr Thr Gln Ser His Arg Arg His Leu Val Glu Phe
1410 1415 1420

Val Thr Trp Ser Thr Pro Gln Leu Tyr His Ile Leu Ala Lys Ser Thr
1425 1430 1435 1440

Ala Leu Ser Met Ile Asp Leu Val Thr Lys Phe Glu Lys Asp His Met
1445 1450 1455

Asn Glu Ile Ser Ala Leu Ile Gly Asp Asp Asp Ile Asn Ser Phe Ile
1460 1465 1470

Thr Glu Phe Leu Leu Ile Glu Pro Arg Leu Phe Thr Ile Tyr Leu Gly
1475 1480 1485

Gln Cys Ala Ala Ile Asn Trp Ala Phe Asp Val His Tyr His Arg Pro
1490 1495 1500

Ser Gly Lys Tyr Gln Met Gly Glu Leu Leu Ser Ser Phe Leu Ser Arg
1505 1510 1515 1520

Met Ser Lys Gly Val Phe Lys Val Leu Val Asn Ala Leu Ser His Pro
1525 1530 1535

Lys Ile Tyr Lys Lys Phe Trp His Cys Gly Ile Ile Glu Pro Ile His
1540 1545 1550

Gly Pro Ser Leu Asp Ala Gln Asn Leu His Thr Thr Val Cys Asn Met
1555 1560 1565

Val Tyr Thr Cys Tyr Met Thr Tyr Leu Asp Leu Leu Leu Asn Glu Glu
1570 1575 1580

Leu Glu Glu Phe Thr Phe Leu Leu Cys Glu Ser Asp Glu Asp Val Val
1585 1590 1595 1600

Pro Asp Arg Phe Asp Asn Ile Gln Ala Lys His Leu Cys Val Leu Ala
1605 1610 1615

Asp Leu Tyr Cys Gln Pro Gly Ala Cys Pro Pro Ile Arg Gly Leu Arg
1620 1625 1630

Pro Val Glu Lys Cys Ala Val Leu Thr Asp His Ile Lys Ala Glu Ala
1635 1640 1645

Arg Leu Ser Pro Ala Gly Ser Ser Trp Asn Ile Asn Pro Ile Ile Val
1650 1655 1660

Asp His Tyr Ser Cys Ser Leu Thr Tyr Leu Arg Arg Gly Ser Ile Lys
1665 1670 1675 1680

Gln Ile Arg Leu Arg Val Asp Pro Gly Phe Ile Phe Asp Ala Leu Ala
1685 1690 1695

Glu Val Asn Val Ser Gln Pro Lys Ile Gly Ser Asn Asn Ile Ser Asn
1700 1705 1710

Met Ser Ile Lys Ala Phe Arg Pro Pro His Asp Asp Val Ala Lys Leu
1715 1720 1725

Leu Lys Asp Ile Asn Thr Ser Lys His Asn Leu Pro Ile Ser Gly Gly
1730 1735 1740

Asn Leu Ala Asn Tyr Glu Ile His Ala Phe Arg Arg Ile Gly Leu Asn
1745 1750 1755 1760

Ser Ser Ala Cys Tyr Lys Ala Val Glu Ile Ser Thr Leu Ile Arg Arg
1765 1770 1775

Cys Leu Glu Pro Gly Glu Asp Gly Leu Phe Leu Gly Glu Gly Ser Gly
1780 1785 1790

Ser Met Leu Ile Thr Tyr Lys Glu Ile Leu Lys Leu Asn Lys Cys Phe
1795 1800 1805

Tyr Asn Ser Gly Val Ser Ala Asn Ser Arg Ser Gly Gln Arg Glu Leu
1810 1815 1820

Ala Pro Tyr Pro Ser Glu Val Gly Leu Val Glu His Arg Met Gly Val
1825 1830 1835 1840

Gly Asn Ile Val Lys Val Leu Phe Asn Gly Arg Pro Glu Val Thr Trp
1845 1850 1855

Val Gly Ser Val Asp Cys Phe Asn Phe Ile Val Ser Asn Ile Pro Thr
1860 1865 1870

Ser Ser Val Gly Phe Ile His Ser Asp Ile Glu Thr Leu Pro Asn Lys
1875 1880 1885

Asp Thr Ile Glu Lys Leu Glu Glu Leu Ala Ala Ile Leu Ser Met Ala
1890 1895 1900

Leu Leu Leu Gly Lys Ile Gly Ser Ile Leu Val Ile Lys Leu Met Pro
1905 1910 1915 1920

Phe Ser Gly Asp Phe Val Gln Gly Phe Ile Ser Tyr Val Gly Ser Tyr
1925 1930 1935

Tyr Arg Glu Val Asn Leu Val Tyr Pro Arg Tyr Ser Asn Phe Ile Ser
1940 1945 1950

Thr Glu Ser Tyr Leu Val Met Thr Asp Leu Lys Ala Asn Arg Leu Met
1955 1960 1965

Asn Pro Glu Lys Ile Lys Gln Gln Ile Ile Glu Ser Ser Val Arg Thr
1970 1975 1980

Ser Pro Gly Leu Ile Gly His Ile Leu Ser Ile Lys Gln Leu Ser Cys
1985 1990 1995 2000

Ile Gln Ala Ile Val Gly Asp Ala Val Ser Arg Gly Asp Ile Asn Pro
2005 2010 2015

Thr Leu Lys Lys Leu Thr Pro Ile Glu Gln Val Leu Ile Asn Cys Gly
2020 2025 2030

Leu Ala Ile Asn Gly Pro Lys Leu Cys Lys Glu Leu Ile His His Asp
2035 2040 2045

Val Ala Ser Gly Gln Asp Gly Leu Leu Asn Ser Ile Leu Ile Leu Tyr
2050 2055 2060

Arg Glu Leu Ala Arg Phe Lys Asp Asn Arg Arg Ser Gln Gln Gly Met
2065 2070 2075 2080

Phe His Ala Tyr Pro Val Leu Val Ser Ser Arg Gln Arg Glu Leu Ile
2085 2090 2095

Ser Arg Ile Thr Arg Lys Phe Trp Gly His Ile Leu Leu Tyr Ser Gly
2100 2105 2110

Asn Arg Lys Leu Ile Asn Lys Phe Ile Gln Asn Leu Lys Ser Gly Tyr

2115 2120 2125

Leu Ile Leu Asp Leu His Gln Asn Ile Phe Val Lys Asn Leu Ser Lys
2130 2135 2140

Ser Glu Lys Gln Ile Ile Met Thr Gly Gly Leu Lys Arg Glu Trp Val
2145 2150 2155 2160

Phe Lys Val Thr Val Lys Glu Thr Lys Glu Trp Tyr Lys Leu Val Gly
2165 2170 2175

Tyr Ser Ala Leu Ile Lys Asp
2180

(2) INFORMATION FOR SEQ ID NO:17:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 15462 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

ACCAAACAAG AGAAGAAACT TGTCTGGGAA TATAAATTTA ACTTTAAATT AACTTAGGAT 60

TAAAGACATT GACTAGAAGG TCAAGAAAAG GGAACTCTAT AATTTCAAAA ATGTTGAGCC 120

TATTTGATAC ATTTAATGCA CGTAGGCAAG AAAACATAAC AAAATCAGCC GGTGGAGCTA 180

TCATTCCTGG ACAGAAAAAT ACTGTCTCTA TATTCGCCCT TGGACCGACA ATAACTGATG 240

ATAATGAGAA AATGACATTA GCTCTTCTAT TTCTATCTCA TTCACTAGAT AATGAGAAAC 300

AACATGCACA AAGGGCAGGG TTCTTGGTGT CTTTATTGTC AATGGCTTAT GCCAATCCAG 360

AGCTCTACCT AACAACAAAT GGAAGTAATG CAGATGTCAA GTATGTCATA TACATGATTG 420

AGAAAGATCT AAAACGGCAA AAGTATGGAG GATTTGTGGT TAAGACGAGA GAGATGATAT 480

ATGAAAAGAC AACTGATTGG ATATTTGGAA GTGACCTGGA TTATGATCAG GAAACTATGT 540

TGCAGAACGG CAGGAACAAT TCAACAATTG AAGACCTTGT CCACACATTT GGGTATCCAT 600

CATGTTTAGG AGCTCTTATA ATACAGATCT GGATAGTTCT GGTCAAAGCT ATCACTAGTA 660

TCTCAGGGTT AAGAAAAGGC TTTTTCACCC GATTGGAAGC TTTCAGACAA GATGGAACAG 720

TGCAGGCAGG GCTGGTATTG AGCGGTGACA CAGTGGATCA GATTGGGTCA ATCATGCGGT 780

CTCAACAGAG CTTGGTAACT CTTATGGTTG AAACATTAAT AACAATGAAT ACCAGCAGAA 840

ATGACCTCAC AACCATAGAA AAGAATATAC AAATTGTTGG CAACTACATA AGAGATGCAG 900

GTCTCGCTTC ATTCTTCAAT ACAATCAGAT ATGGAATTGA GACCAGAATG GCAGCTTTGA 960

CTCTATCCAC TCTCAGACCA GATATCAATA GATTAAAAGC TTTGATGGAA CTGTATTTAT 1020

CAAAGGGACC ACGCGCTCCT TTCATCTGTA TCCTCAGAGA TCCTATACAT GGTGAGTTCG 1080

CACCAGGCAA CTATCCTGCC ATATGGAGCT ATGCAATGGG GGTGGCAGTT GTACAAAATA 1140

GAGCCATGCA ACAGTATGTG ACGGGAAGAT CATATCTAGA CATTGATATG TTCCAGCTAG 1200

GACAAGCAGT AGCACGTGAT GCCGAAGCTC AAATGAGCTC AACACTGGAA GATGAACTTG 1260

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CAGAACAATT CGAACATAGA GCAGATCAAG AACAAAATGG AGAACCTCAA TCATCCATAA 1440

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GGTAAATTTA GAGTCTGCTT GAAACTCAAT CAATAGAGAG TTGATGGAAA GCGATGCTAA 1800

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CAAACCAACA GAAACAAGTG AGAAAGATAG TGGATCAACT GACAAAAATA GACAGTCCGG 2040

GTCATCACAC GAATGTACAA CAGAAGCAAA AGATAGAAAT ATTGATCAGG AAACTGTACA 2100

GAGAGGACCT GGGAGAAGAA GCAGCTCAGA TAGTAGAGCT GAGACTGTGG TCTCTGGAGG 2160

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CAATGAAATT AGAAAGATGG ATAAGGACTC TATTGAGGGG AAAATGCGAC AATCTGCAAA 2280

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ATGTAGTGAG ATTTTTTGAT TCATTAAGAG AAGTGATGGA TGATCTAGGT CATGAACTTA 11100

AATTAAATGA AACGATTATA AGTAGCAAGA TGTTCATATA TAGCAAAAGA ATCTATTATG 11160

ATGGGAGAAT TCTTCCTCAA GCTCTAAAAG CATTATCTAG ATGTGTCTTC TGGTCAGAGA 11220

CAGTAATAGA CGAAACAAGA TCAGCATCTT CAAATTTGGC AACATCATTT GCAAAAGCAA 11280

TTGAGAATGG TTATTCACCT GTTCTAGGAT ATGCATGCTC AATTTTTAAG AACATTCAAC 11340

AACTATATAT TGCCCTTGGG ATGAATATCA ATCCAACTAT AACACAGAAT ATCAGAGATC 11400

AGTATTTTAG GAATCCAAAT TGGATGCAAT ATGCCTCTTT AATACCTGCT AGTGTTGGGG 11460

GATTCAATTA CATGGCCATG TCAAGATGTT TTGTAAGGAA TATTGGTGAT CCATCAGTTG 11520

CCGCATTGGC TGATATTAAA AGATTTATTA AGGCGAATCT ATTAGACCGA AGTGTTCTTT 11580

ATAGGATTAT GAATCAAGAA CCAGGTGAGT CATCTTTTTT GGACTGGGCT TCAGATCCAT 11640

ATTCATGCAA TTTACCACAA TCTCAAAATA TAACCACCAT GATAAAAAAT ATAACAGCAA 11700

GGAATGTATT ACAAGATTCA CCAAATCCAT TATTATCTGG ATTATTCACA AATACAATGA 11760

TAGAAGAAGA TGAAGAATTA GCTGAGTTCC TGATGGACAG GAAGGTAATT CTCCCTAGAG 11820

TTGCACATGA TATTCTAGAT AATTCTCTCA CAGGAATTAG AAATGCCATA GCTGGAATGT 11880

TAGATACGAC AAAATCACTA ATTCGGGTTG GCATAAATAG AGGAGGACTG ACATATAGTT 11940

TGTTGAGGAA AATCAGTAAT TACGATCTAG TACAATATGA AACACTAAGT AGGACTTTGC 12000

GACTAATTGT AAGTGATAAA ATCAAGTATG AAGATATGTG TTCGGTAGAC CTTGCCATAG 12060

CATTGCGACA AAAGATGTGG ATTCATTTAT CAGGAGGAAG GATGATAAGT GGACTTGAAA 12120

CGCCTGACCC ATTAGAATTA CTATCTGGGG TAGTAATAAC AGGATCAGAA CATTGTAAAA 12180

TATGTTATTC TTCAGATGGC ACAAACCCAT ATACTTGGAT GTATTTACCC GGTAATATCA 12240

AAATAGGATC AGCAGAAACA GGTATATCGT CATTAAGAGT TCCTTATTTT GGATCAGTCA 12300

CTGATGAAAG ATCTGAAGCA CAATTAGGAT ATATCAAGAA TCTTAGTAAA CCTGCAAAAG 12360

CCGCAATAAG AATAGCAATG ATATATACAT GGGCATTTGG TAATGATGAG ATATCTTGGA 12420

TGGAAGCCTC ACAGATAGCA CAAACACGTG CAAATTTTAC ACTAGATAGT CTCAAAATTT 12480

TAACACCGGT AGCTACATCA ACAAATTTAT CACACAGATT AAAGGATACT GCAACTCAGA 12540

TGAAATTCTC CAGTACATCA TTGATCAGAG TCAGCAGATT CATAACAATG TCCAATGATA 12600

ACATGTCTAT CAAAGAAGCT AATGAAACCA AAGATACTAA TCTTATTTAT CAACAAATAA 12660

TGTTAACAGG ATTAAGTGTT TTCGAATATT TATTTAGATT AAAAGAAACC ACAGGACACA 12720

ACCCTATAGT TATGCATCTG CACATAGAAG ATGAGTGTTG TATTAAAGAA AGTTTTAATG 12780

ATGAACATAT TAATCCAGAG TCTACATTAG AATTAATTCG ATATCCTGAA AGTAATGAAT 12840

TTATTTATGA TAAAGACCCA CTCAAAGATG TGGACTTATC AAAACTTATG GTTATTAAAG 12900

ACCATTCTTA CACAATTGAT ATGAATTATT GGGATGATAC TGACATCATA CATGCAATTT 12960

CAATATGTAC TGCAATTACA ATAGCAGATA CTATGTCACA ATTAGATCGA GATAATTTAA 13020

AAGAGATAAT AGTTATTGCA AATGATGATG ATATTAATAG CTTAATCACT GAATTTTTGA 13080

CTCTTGACAT ACTTGTATTT CTCAAGACAT TTGGTGGATT ATTAGTAAAT CAATTTGCAT 13140

ACACTCTTTA TAGTCTAAAA ATAGAAGGTA GGGATCTCAT TTGGGATTAT ATAATGAGAA 13200

CACTGAGAGA TACTTCCCAT TCAATATTAA AAGTATTATC TAATGCATTA TCTCATCCTA 13260

AAGTATTCAA GAGGTTCTGG GATTGTGGAG TTTTAAACCC TATTTATGGT CCTAATACTG 13320

CTAGTCAAGA CCAGATAAAA CTTGCCCTAT CTATATGTGA ATATTCACTA GATCTATTTA 13380

TGAGAGAATG GTTGAATGGT GTATCACTTG AAATATACAT TTGTGACAGC GATATGGAAG 13440

TTGCAAATGA TAGGAAACAA GCCTTTATTT CTAGACACCT TTCATTTGTT TGTTGTTTAG 13500

CAGAAATTGC ATCTTTCGGA CCTAACCTGT TAAACTTAAC ATACTTGGAG AGACTTGATC 13560

TATTGAAACA ATATCTTGAA TTAAATATTA AAGAAGACCC TACTCTTAAA TATGTACAAA 13620

TATCTGGATT ATTAATTAAA TCGTTCCCAT CAACTGTAAC ATACGTAAGA AAGACTGCAA 13680

TCAAATATCT AAGGATTCGC GGTATTAGTC CACCTGAGGT AATTGATGAT TGGGATCCGG 13740

TAGAAGATGA AAATATGCTG GATAACATTG TCAAAACTAT AAATGATAAC TGTAATAAAG 13800

ATAATAAAGG GAATAAAATT AACAATTTCT GGGGACTAGC ACTTAAGAAC TATCAAGTCC 13860

TTAAAATCAG ATCTATAACA AGTGATTCTG ATGATAATGA TAGACTAGAT GCTAATACAA 13920

GTGGTTTGAC ACTTCCTCAA GGAGGGAATT ATCTATCGCA TCAATTGAGA TTATTCGGAA 13980

TCAACAGCAC TAGTTGTCTG AAAGCTCTTG AGTTATCACA AATTTTAATG AAGGAAGTCA 14040

ATAAAGACAA GGACAGGCTC TTCCTGGGAG AAGGAGCAGG AGCTATGCTA GCATGTTATG 14100

ATGCCACATT AGGACCTGCA GTTAATTATT ATAATTCAGG TTTGAATATA ACAGATGTAA 14160

TTGGTCAACG AGAATTGAAA ATATTTCCTT CAGAGGTATC ATTAGTAGGT AAAAAATTAG 14220

GAAATGTGAC ACAGATTCTT AACAGGGTAA AAGTACTGTT CAATGGGAAT CCTAATTCAA 14280

CATGGATAGG AAATATGGAA TGTGAGAGCT TAATATGGAG TGAATTAAAT GATAAGTCCA 14340

TTGGATTAGT ACATTGTGAT ATGGAAGGAG CTATCGGTAA ATCAGAAGAA ACTGTTCTAC 14400

ATGAACATTA TAGTGTTATA AGAATTACAT ACTTGATTGG GGATGATGAT GTTGTTTTAG 14460

TTTCCAAAAT TATACCTACA ATCACTCCGA ATTGGTCTAG AATACTTTAT CTATATAAAT 14520

TATATTGGAA AGATGTAAGT ATAATATCAC TCAAAACTTC TAATCCTGCA TCAACAGAAT 14580

TATATCTAAT TTCGAAAGAT GCATATTGTA CTATAATGGA ACCTAGTGAA ATTGTTTTAT 14640

CAAAACTTAA AAGATTGTCA CTCTTGGAAG AAAATAATCT ATTAAAATGG ATCATTTTAT 14700

CAAAGAAGAG GAATAATGAA TGGTTACATC ATGAAATCAA AGAAGGAGAA AGAGATTATG 14760

GAATCATGAG ACCATATCAT ATGGCACTAC AAATCTTTGG ATTTCAAATC AATTTAAATC 14820

ATCTGGCGAA AGAATTTTTA TCAACCCCAG ATCTGACTAA TATCAACAAT ATAATCCAAA 14880

GTTTTCAGCG AACAATAAAG GATGTTTTAT TTGAATGGAT TAATATAACT CATGATGATA 14940

AGAGACATAA ATTAGGCGGA AGATATAACA TATTCCCACT GAAAAATAAG GGAAAGTTAA 15000

GACTGCTATC GAGAAGACTA GTATTAAGTT GGATTTCATT ATCATTATCG ACTCGATTAC 15060

TTACAGGTCG CTTTCCTGAT GAAAAATTTG AACATAGAGC ACAGACTGGA TATGTATCAT 15120

TAGCTGATAC TGATTTAGAA TCATTAAAGT TATTGTCGAA AAACATCATT AAGAATTACA 15180

GAGAGTGTAT AGGATCAATA TCATATTGGT TTCTAACCAA AGAAGTTAAA ATACTTATGA 15240

AATTGATTGG TGGTGCTAAA TTATTAGGAA TTCCCAGACA ATATAAAGAA CCCGAAGACC 15300

AGTTATTAGA AAACTACAAT CAACATGATG AATTTGATAT CGATTAAAAC ATAAATACAA 15360

TGAAGATATA TCCTAACCTT TATCTTTAAG CCTAGGAATA GACAAAAAGT AAGAAAAACA 15420

TGTAATATAT ATATACCAAA CAGAGTTCTT CTCTTGTTTG GT 15462

(2) INFORMATION FOR SEQ ID NO:18:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2233 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

Met Asp Thr Glu Ser Asn Asn Gly Thr Val Ser Asp Ile Leu Tyr Pro
1 5 10 15

Glu Cys His Leu Asn Ser Pro Ile Val Lys Gly Lys Ile Ala Gln Leu
20 25 30

His Thr Ile Met Ser Leu Pro Gln Pro Tyr Asp Met Asp Asp Asp Ser
35 40 45

Ile Leu Val Ile Thr Arg Gln Lys Ile Lys Leu Asn Lys Leu Asp Lys
50 55 60

Arg Gln Arg Ser Ile Arg Arg Leu Lys Leu Ile Leu Thr Glu Lys Val
65 70 75 80

Asn Asp Leu Gly Lys Tyr Thr Phe Ile Arg Tyr Pro Glu Met Ser Lys
85 90 95

Glu Met Phe Lys Leu Tyr Ile Pro Gly Ile Asn Ser Lys Val Thr Glu
100 105 110

Leu Leu Leu Lys Ala Asp Arg Thr Tyr Ser Gln Met Thr Asp Gly Leu
115 120 125

Arg Asp Leu Trp Ile Asn Val Leu Ser Lys Leu Ala Ser Lys Asn Asp
130 135 140

Gly Ser Asn Tyr Asp Leu Asn Glu Glu Ile Asn Asn Ile Ser Lys Val
145 150 155 160

His Thr Thr Tyr Lys Ser Asp Lys Trp Tyr Asn Pro Phe Lys Thr Trp
165 170 175

Phe Thr Ile Lys Tyr Asp Met Arg Arg Leu Gln Lys Ala Arg Asn Glu
180 185 190

Ile Thr Phe Asn Val Gly Lys Asp Tyr Asn Leu Leu Glu Asp Gln Lys
195 200 205

Asn Phe Leu Leu Ile His Pro Glu Leu Val Leu Ile Leu Asp Lys Gln
210 215 220

Asn Tyr Asn Gly Tyr Leu Ile Thr Pro Glu Leu Val Leu Met Tyr Cys
225 230 235 240

Asp Val Val Glu Gly Arg Trp Asn Ile Ser Ala Cys Ala Lys Leu Asp
245 250 255

Pro Lys Leu Gln Ser Met Tyr Gln Lys Gly Asn Asn Leu Trp Glu Val
260 265 270

Ile Asp Lys Leu Phe Pro Ile Met Gly Glu Lys Thr Phe Asp Val Ile
275 280 285

Ser Leu Leu Glu Pro Leu Ala Leu Ser Leu Ile Gln Thr His Asp Pro
290 295 300

Val Lys Gln Leu Arg Gly Ala Phe Leu Asn His Val Leu Ser Glu Met
305 310 315 320

Glu Leu Ile Phe Glu Ser Arg Glu Ser Ile Lys Glu Phe Leu Ser Val
325 330 335

Asp Tyr Ile Asp Lys Ile Leu Asp Ile Phe Asn Lys Ser Thr Ile Asp

340 345 350

Glu Ile Ala Glu Ile Phe Ser Phe Phe Arg Thr Phe Gly His Pro Pro
355 360 365

Leu Glu Ala Ser Ile Ala Ala Glu Lys Val Arg Lys Tyr Met Tyr Ile
370 375 380

Gly Lys Gln Leu Lys Phe Asp Thr Ile Asn Lys Cys His Ala Ile Phe
385 390 395 400

Cys Thr Ile Ile Ile Asn Gly Tyr Arg Glu Arg His Gly Gly Gln Trp
405 410 415

Pro Pro Val Thr Leu Pro Asp His Ala His Glu Phe Ile Ile Asn Ala
420 425 430

Tyr Gly Ser Asn Ser Ala Ile Ser Tyr Glu Asn Ala Val Asp Tyr Tyr
435 440 445

Gln Ser Phe Ile Gly Ile Lys Phe Asn Lys Phe Ile Glu Pro Gln Leu
450 455 460

Asp Glu Asp Leu Thr Ile Tyr Met Lys Asp Lys Ala Leu Ser Pro Lys
465 470 475 480

Lys Ser Asn Trp Asp Thr Val Tyr Pro Ala Ser Asn Leu Leu Tyr Arg
485 490 495

Thr Asn Ala Ser Asn Glu Ser Arg Arg Leu Val Glu Val Phe Ile Ala
500 505 510

Asp Ser Lys Phe Asp Pro His Gln Ile Leu Asp Tyr Val Glu Ser Gly
515 520 525

Asp Trp Leu Asp Asp Pro Glu Phe Asn Ile Ser Tyr Ser Leu Lys Glu
530 535 540

Lys Glu Ile Lys Gln Glu Gly Arg Leu Phe Ala Lys Met Thr Tyr Lys
545 550 555 560

Met Arg Ala Thr Gln Val Leu Ser Glu Thr Leu Leu Ala Asn Asn Ile
565 570 575

Gly Lys Phe Phe Gln Glu Asn Gly Met Val Lys Gly Glu Ile Glu Leu
580 585 590

Leu Lys Arg Leu Thr Thr Ile Ser Ile Ser Gly Val Pro Arg Tyr Asn
595 600 605

Glu Val Tyr Asn Asn Ser Lys Ser His Thr Asp Asp Leu Lys Thr Tyr
610 615 620

Asn Lys Ile Ser Asn Leu Asn Leu Ser Ser Asn Gln Lys Ser Lys Lys
625 630 635 640

Phe Glu Phe Lys Ser Thr Asp Ile Tyr Asn Asp Gly Tyr Glu Thr Val
645 650 655

Ser Cys Phe Leu Thr Thr Asp Leu Lys Lys Tyr Cys Leu Asn Trp Arg
660 665 670

Tyr Glu Ser Thr Ala Leu Phe Gly Glu Thr Cys Asn Gln Ile Phe Gly
675 680 685

Leu Asn Lys Leu Phe Asn Trp Leu His Pro Arg Leu Glu Gly Ser Thr
690 695 700

Ile Tyr Val Gly Asp Pro Tyr Cys Pro Pro Ser Asp Lys Glu His Ile
705 710 715 720

Ser Leu Glu Asp His Pro Asp Ser Gly Phe Tyr Val His Asn Pro Arg
725 730 735

Gly Gly Ile Glu Gly Phe Cys Gln Lys Leu Trp Thr Leu Ile Ser Ile
740 745 750

Ser Ala Ile His Leu Ala Ala Val Arg Ile Gly Val Arg Val Thr Ala
755 760 765

Met Val Gln Gly Asp Asn Gln Ala Ile Ala Val Thr Thr Arg Val Pro
770 775 780

Asn Asn Tyr Asp Tyr Arg Val Lys Lys Glu Ile Val Tyr Lys Asp Val
785 790 795 800

Val Arg Phe Phe Asp Ser Leu Arg Glu Val Met Asp Asp Leu Gly His
805 810 815

Glu Leu Lys Leu Asn Glu Thr Ile Ile Ser Ser Lys Met Phe Ile Tyr
820 825 830

Ser Lys Arg Ile Tyr Tyr Asp Gly Arg Ile Leu Pro Gln Ala Leu Lys
835 840 845

Ala Leu Ser Arg Cys Val Phe Trp Ser Glu Thr Val Ile Asp Glu Thr
850 855 860

Arg Ser Ala Ser Ser Asn Leu Ala Thr Ser Phe Ala Lys Ala Ile Glu
865 870 875 880

Asn Gly Tyr Ser Pro Val Leu Gly Tyr Ala Cys Ser Ile Phe Lys Asn
885 890 895

Ile Gln Gln Leu Tyr Ile Ala Leu Gly Met Asn Ile Asn Pro Thr Ile
900 905 910

Thr Gln Asn Ile Arg Asp Gln Tyr Phe Arg Asn Pro Asn Trp Met Gln
915 920 925

Tyr Ala Ser Leu Ile Pro Ala Ser Val Gly Gly Phe Asn Tyr Met Ala
930 935 940

Met Ser Arg Cys Phe Val Arg Asn Ile Gly Asp Pro Ser Val Ala Ala
945 950 955 960

Leu Ala Asp Ile Lys Arg Phe Ile Lys Ala Asn Leu Leu Asp Arg Ser
965 970 975

Val Leu Tyr Arg Ile Met Asn Gln Glu Pro Gly Glu Ser Ser Phe Leu
980 985 990

Asp Trp Ala Ser Asp Pro Tyr Ser Cys Asn Leu Pro Gln Ser Gln Asn
995 1000 1005

Ile Thr Thr Met Ile Lys Asn Ile Thr Ala Arg Asn Val Leu Gln Asp
1010 1015 1020

Ser Pro Asn Pro Leu Leu Ser Gly Leu Phe Thr Asn Thr Met Ile Glu
1025 1030 1035 1040

Glu Asp Glu Glu Leu Ala Glu Phe Leu Met Asp Arg Lys Val Ile Leu
1045 1050 1055

Pro Arg Val Ala His Asp Ile Leu Asp Asn Ser Leu Thr Gly Ile Arg
1060 1065 1070

Asn Ala Ile Ala Gly Met Leu Asp Thr Thr Lys Ser Leu Ile Arg Val
1075 1080 1085

Gly Ile Asn Arg Gly Gly Leu Thr Tyr Ser Leu Leu Arg Lys Ile Ser
1090 1095 1100

Asn Tyr Asp Leu Val Gln Tyr Glu Thr Leu Ser Arg Thr Leu Arg Leu
1105 1110 1115 1120

Ile Val Ser Asp Lys Ile Lys Tyr Glu Asp Met Cys Ser Val Asp Leu
1125 1130 1135

Ala Ile Ala Leu Arg Gln Lys Met Trp Ile His Leu Ser Gly Gly Arg
1140 1145 1150

Met Ile Ser Gly Leu Glu Thr Pro Asp Pro Leu Glu Leu Leu Ser Gly
1155 1160 1165

Val Val Ile Thr Gly Ser Glu His Cys Lys Ile Cys Tyr Ser Ser Asp

1170 1175 1180

Gly Thr Asn Pro Tyr Thr Trp Met Tyr Leu Pro Gly Asn Ile Lys Ile
1185 1190 1195 1200

Gly Ser Ala Glu Thr Gly Ile Ser Ser Leu Arg Val Pro Tyr Phe Gly
1205 1210 1215

Ser Val Thr Asp Glu Arg Ser Glu Ala Gln Leu Gly Tyr Ile Lys Asn
1220 1225 1230

Leu Ser Lys Pro Ala Lys Ala Ala Ile Arg Ile Ala Met Ile Tyr Thr
1235 1240 1245

Trp Ala Phe Gly Asn Asp Glu Ile Ser Trp Met Glu Ala Ser Gln Ile
1250 1255 1260

Ala Gln Thr Arg Ala Asn Phe Thr Leu Asp Ser Leu Lys Ile Leu Thr
1265 1270 1275 1280

Pro Val Ala Thr Ser Thr Asn Leu Ser His Arg Leu Lys Asp Thr Ala
1285 1290 1295

Thr Gln Met Lys Phe Ser Ser Thr Ser Leu Ile Arg Val Ser Arg Phe
1300 1305 1310

Ile Thr Met Ser Asn Asp Asn Met Ser Ile Lys Glu Ala Asn Glu Thr
1315 1320 1325

Lys Asp Thr Asn Leu Ile Tyr Gln Gln Ile Met Leu Thr Gly Leu Ser
1330 1335 1340

Val Phe Glu Tyr Leu Phe Arg Leu Lys Glu Thr Thr Gly His Asn Pro
1345 1350 1355 1360

Ile Val Met His Leu His Ile Glu Asp Glu Cys Cys Ile Lys Glu Ser
1365 1370 1375

Phe Asn Asp Glu His Ile Asn Pro Glu Ser Thr Leu Glu Leu Ile Arg
1380 1385 1390

Tyr Pro Glu Ser Asn Glu Phe Ile Tyr Asp Lys Asp Pro Leu Lys Asp
1395 1400 1405

Val Asp Leu Ser Lys Leu Met Val Ile Lys Asp His Ser Tyr Thr Ile
1410 1415 1420

Asp Met Asn Tyr Trp Asp Asp Thr Asp Ile Ile His Ala Ile Ser Ile
1425 1430 1435 1440

Cys Thr Ala Ile Thr Ile Ala Asp Thr Met Ser Gln Leu Asp Arg Asp
1445 1450 1455

Asn Leu Lys Glu Ile Ile Val Ile Ala Asn Asp Asp Asp Ile Asn Ser
1460 1465 1470

Leu Ile Thr Glu Phe Leu Thr Leu Asp Ile Leu Val Phe Leu Lys Thr
1475 1480 1485

Phe Gly Gly Leu Leu Val Asn Gln Phe Ala Tyr Thr Leu Tyr Ser Leu
1490 1495 1500

Lys Ile Glu Gly Arg Asp Leu Ile Trp Asp Tyr Ile Met Arg Thr Leu
1505 1510 1515 1520

Arg Asp Thr Ser His Ser Ile Leu Lys Val Leu Ser Asn Ala Leu Ser
1525 1530 1535

His Pro Lys Val Phe Lys Arg Phe Trp Asp Cys Gly Val Leu Asn Pro
1540 1545 1550

Ile Tyr Gly Pro Asn Thr Ala Ser Gln Asp Gln Ile Lys Leu Ala Leu
1555 1560 1565

Ser Ile Cys Glu Tyr Ser Leu Asp Leu Phe Met Arg Glu Trp Leu Asn
1570 1575 1580

Gly Val Ser Leu Glu Ile Tyr Ile Cys Asp Ser Asp Met Glu Val Ala
1585 1590 1595 1600

Asn Asp Arg Lys Gln Ala Phe Ile Ser Arg His Leu Ser Phe Val Cys
1605 1610 1615

Cys Leu Ala Glu Ile Ala Ser Phe Gly Pro Asn Leu Leu Asn Leu Thr
1620 1625 1630

Tyr Leu Glu Arg Leu Asp Leu Leu Lys Gln Tyr Leu Glu Leu Asn Ile
1635 1640 1645

Lys Glu Asp Pro Thr Leu Lys Tyr Val Gln Ile Ser Gly Leu Leu Ile
1650 1655 1660

Lys Ser Phe Pro Ser Thr Val Thr Tyr Val Arg Lys Thr Ala Ile Lys
1665 1670 1675 1680

Tyr Leu Arg Ile Arg Gly Ile Ser Pro Pro Glu Val Ile Asp Asp Trp
1685 1690 1695

Asp Pro Val Glu Asp Glu Asn Met Leu Asp Asn Ile Val Lys Thr Ile
1700 1705 1710

Asn Asp Asn Cys Asn Lys Asp Asn Lys Gly Asn Lys Ile Asn Asn Phe
1715 1720 1725

Trp Gly Leu Ala Leu Lys Asn Tyr Gln Val Leu Lys Ile Arg Ser Ile
1730 1735 1740

Thr Ser Asp Ser Asp Asp Asn Asp Arg Leu Asp Ala Asn Thr Ser Gly
1745 1750 1755 1760

Leu Thr Leu Pro Gln Gly Gly Asn Tyr Leu Ser His Gln Leu Arg Leu
1765 1770 1775

Phe Gly Ile Asn Ser Thr Ser Cys Leu Lys Ala Leu Glu Leu Ser Gln
1780 1785 1790

Ile Leu Met Lys Glu Val Asn Lys Asp Lys Asp Arg Leu Phe Leu Gly
1795 1800 1805

Glu Gly Ala Gly Ala Met Leu Ala Cys Tyr Asp Ala Thr Leu Gly Pro
1810 1815 1820

Ala Val Asn Tyr Tyr Asn Ser Gly Leu Asn Ile Thr Asp Val Ile Gly
1825 1830 1835 1840

Gln Arg Glu Leu Lys Ile Phe Pro Ser Glu Val Ser Leu Val Gly Lys
1845 1850 1855

Lys Leu Gly Asn Val Thr Gln Ile Leu Asn Arg Val Lys Val Leu Phe
1860 1865 1870

Asn Gly Asn Pro Asn Ser Thr Trp Ile Gly Asn Met Glu Cys Glu Ser
1875 1880 1885

Leu Ile Trp Ser Glu Leu Asn Asp Lys Ser Ile Gly Leu Val His Cys
1890 1895 1900

Asp Met Glu Gly Ala Ile Gly Lys Ser Glu Glu Thr Val Leu His Glu
1905 1910 1915 1920

His Tyr Ser Val Ile Arg Ile Thr Tyr Leu Ile Gly Asp Asp Asp Val
1925 1930 1935

Val Leu Val Ser Lys Ile Ile Pro Thr Ile Thr Pro Asn Trp Ser Arg
1940 1945 1950

Ile Leu Tyr Leu Tyr Lys Leu Tyr Trp Lys Asp Val Ser Ile Ile Ser
1955 1960 1965

Leu Lys Thr Ser Asn Pro Ala Ser Thr Glu Leu Tyr Leu Ile Ser Lys
1970 1975 1980

Asp Ala Tyr Cys Thr Ile Met Glu Pro Ser Glu Ile Val Leu Ser Lys
1985 1990 1995 2000

Leu Lys Arg Leu Ser Leu Leu Glu Glu Asn Asn Leu Leu Lys Trp Ile

2005 2010 2015

Ile Leu Ser Lys Lys Arg Asn Asn Glu Trp Leu His His Glu Ile Lys
2020 2025 2030

Glu Gly Glu Arg Asp Tyr Gly Ile Met Arg Pro Tyr His Met Ala Leu
2035 2040 2045

Gln Ile Phe Gly Phe Gln Ile Asn Leu Asn His Leu Ala Lys Glu Phe
2050 2055 2060

Leu Ser Thr Pro Asp Leu Thr Asn Ile Asn Asn Ile Ile Gln Ser Phe
2065 2070 2075 2080

Gln Arg Thr Ile Lys Asp Val Leu Phe Glu Trp Ile Asn Ile Thr His
2085 2090 2095

Asp Asp Lys Arg His Lys Leu Gly Gly Arg Tyr Asn Ile Phe Pro Leu
2100 2105 2110

Lys Asn Lys Gly Lys Leu Arg Leu Leu Ser Arg Arg Leu Val Leu Ser
2115 2120 2125

Trp Ile Ser Leu Ser Leu Ser Thr Arg Leu Leu Thr Gly Arg Phe Pro
2130 2135 2140

Asp Glu Lys Phe Glu His Arg Ala Gln Thr Gly Tyr Val Ser Leu Ala
2145 2150 2155 2160

Asp Thr Asp Leu Glu Ser Leu Lys Leu Leu Ser Lys Asn Ile Ile Lys
2165 2170 2175

Asn Tyr Arg Glu Cys Ile Gly Ser Ile Ser Tyr Trp Phe Leu Thr Lys
2180 2185 2190

Glu Val Lys Ile Leu Met Lys Leu Ile Gly Gly Ala Lys Leu Leu Gly
2195 2200 2205

Ile Pro Arg Gln Tyr Lys Glu Pro Glu Asp Gln Leu Leu Glu Asn Tyr
2210 2215 2220

Asn Gln His Asp Glu Phe Asp Ile Asp
2225 2230

(2) INFORMATION FOR SEQ ID NO:19:

(i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 15462 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

ACCAAACAAG AGAAGAAACT TGCTTGGTAA TATAAATTTA ACTTAAAATT AACTTAGGAT 60

TTAAGACATT GACTAGAAGG TCAAGAAAAG GGAACTCTAT AATTTCAAAA ATGTTGAGCC 120

TATTTGATAC ATTTAATGCA CGTAGGCAAG AAAACATAAC AAAATCAGCC GGTGGAGCTA 180

TCATTCCTGG ACAGAAAAAT ACTGTCTCTA TATTCGCCCT TGGACCGACA ATAACTGATG 240

ATAATGAGAA AATGACATTA GCTCTTCTAT TTCTATCTCA TTCACTAGAT AATGAGAAAC 300

AACATGCACA AAGGGCAGGG TTCTTGGTGT CTTTATTGTC AATGGCTTAT GCCAATCCAG 360

AGCTCTACCT AACAACAAAT GGAAGTAATG CAGATGCCAA GTATGTCATA TACATGATTG 420

AGAAAGATCT AAAACGGCAA AAGTATGGAG GATTTGTGGT TAAGACGAGA GAGATGATAT 480

ATGAAAAGAC AACTGATTGG ATATTTGGAA GTGACCTGGA TTATGATCAG GAAACTATGT 540

TGCAGAACGG CAGGAACAAT TCAACAATTG AAGACCTTGT CCACACATTT GGGTATCCAT 600

CATGTTTAGG AGCTCTTATA ATACAGATCT GGATAGTTCT GGTCAAAGCT ATCACTAGTA 660

TCTCAGGGTT AAGAAAAGGC TTTTTCACCC GATTGGAAGC TTTCAGACAA GATGGAACAG 720

TGCAGGCAGG GCTGGTATTG AGCGGTGACA CAGTGGATCA GATTGGGTCA ATCATGCGGT 780

CTCAACAGAG CTTGGTAACT CTTATGGTTG AAACATTAAT AACAATGAAT ACCAGCAGAA 840

ATGACCTCAC AACCATAGAA AAGAATATAC AAATTGTTGG CAACTACATA AGAGATGCAG 900

GTCTCGCTTC ATTCTTCAAT ACAATCAGAT ATGGAATTGA GACCAGAATG GCAGCTTTGA 960

CTCTATCCAC TCTCAGACCA GATATCAATA GATTAAAAGC TTTGATGGAA CTGTATTTAT 1020

CAAAGGGACC ACGCGCTCCT TTCATCTGTA TCCTCAGAGA TCCTATACAT GGTGAGTTCG 1080

CACCAGGCAA CTATCCTGCC ATATGGAGCT ATGCAATGGG GGTGGCAGTT GTACAAAATA 1140

GAGCCATGCA ACAGTATGTG ACGGGAAGAT CATATCTAGA CATTGATATG TTCCAGCTAG 1200

GACAAGCAGT AGCACGTGAT GCCGAAGCTC AAATGAGCTC AACACTGGAA GATGAACTTG 1260

GAGTGACACA CGAAGCTAAA GAAAGCTTGA AGAGACATAT AAGGAACATA AACAGTTCAG 1320

AGACATCTTT CCACAAACCG ACAGGTGGAT CAGCCATAGA GATGGCAATA GATGAAGAGC 1380

CAGAACAATT CGAACATAGA GCAGATCAAG AACAAAATGG AGAACCTCAA TCATCCATAA 1440

TTCAATATGC CTGGGCAGAA GGAAATAGAA GCGATGATCA GACTGAGCAA GCTACAGAAT 1500

CTGACAATAT CAAGACCGAA CAACAAAACA TCAGAGACAG ACTAAACAAG AGACTCAACG 1560

ACAAGAAGAA ACAAAGCAGT CAACCACCCA CTAATCCCAC AAACAGAACA AACCAGGACG 1620

AAATAGATGA TCTGTTTAAC GCATTTGGAA GCAACTAATC GAATCAACAT TTTAATCTAA 1680

ATCAATAATA AATAAGAAAA ACTTAGGATT AAAGAATCCT ATCATACCGG AATATAGGGT 1740

GGTAAATTTA GAGTCTGCTT GAAACTCAAT CAATAGAGAG TTGATGGAAA GCGATGCTAA 1800

AAACTATCAA ATCATGGATT CTTGGGAAGA GGAATCAAGA GATAAATCAA CTAATATCTC 1860

CTCGGCCCTC AACATCATTG AATTCATACT CAGCACCGAC CCCCAAGAAG ACTTATCGGA 1920

AAACGACACA ATCAACACAA GAACCCAGCA ACTCAGTGCC ACCATCTGTC AACCAGAAAT 1980

CAAACCAACA GAAACAAGTG AGAAAGATAG TGGATCAACT GACAAAAATA GACAGTCTGG 2040

GTCATCACAC GAATGTACAA CAGAAGCAAA AGATAGAAAC ATTGATCAGG AAACTGTACA 2100

GAGAGGACCT GGGAGAAGAA GCAGCTCAGA TAGTAGAGCT GAGACTGTGG TCTCTGGAGG 2160

AATCCCCAGA AGCATCACAG ATTCTAAAAA TGGAACCCAA AACACGGAGG ATATTGATCT 2220

CAATGAAATT AGAAAGATGG ATAAGGACTC TATTGAGGGG AAAATGCGAC AATCTGCAAA 2280

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TGAAGATATA TCCTAACCTT TATCTTTAAG CCTAGGAATA GACAAAAAGT AAGAAAAACA 15420

TGTAATATAT ATATACCAAA CAGAGTTCTT CTCTTGTTTG GT 15462

(2) INFORMATION FOR SEQ ID NO:20:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2233 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:

Met Asp Thr Glu Ser Asn Asn Gly Thr Val Ser Asp Ile Leu Tyr Pro
1 5 10 15

Glu Cys His Leu Asn Ser Pro Ile Val Lys Gly Lys Ile Ala Gln Leu
20 25 30

His Thr Ile Met Ser Leu Pro Gln Pro Tyr Asp Met Asp Asp Asp Ser
35 40 45

Ile Leu Val Ile Thr Arg Gln Lys Ile Lys Leu Asn Lys Leu Asp Lys
50 55 60

Arg Gln Arg Ser Ile Arg Arg Leu Lys Leu Ile Leu Thr Glu Lys Val
65 70 75 80

Asn Asp Leu Gly Lys Tyr Thr Phe Ile Arg Tyr Pro Glu Met Ser Lys
85 90 95

Glu Met Phe Lys Leu Tyr Ile Pro Gly Ile Asn Ser Lys Val Thr Glu
100 105 110

Leu Leu Leu Lys Ala Asp Arg Thr Tyr Ser Gln Met Thr Asp Gly Leu
115 120 125

Arg Asp Leu Trp Ile Asn Val Leu Ser Lys Leu Ala Ser Lys Asn Asp
130 135 140

Gly Ser Asn Tyr Asp Leu Asn Glu Glu Ile Asn Asn Ile Ser Lys Val
145 150 155 160

His Thr Thr Tyr Lys Ser Asp Lys Trp Tyr Asn Pro Phe Lys Thr Trp
165 170 175

Phe Thr Ile Lys Tyr Asp Met Arg Arg Leu Gln Lys Ala Arg Asn Glu

180 185 190

Ile Thr Phe Asn Val Gly Lys Asp Tyr Asn Leu Leu Glu Asp Gln Lys
195 200 205

Asn Phe Leu Leu Ile His Pro Glu Leu Val Leu Ile Leu Asp Lys Gln
210 215 220

Asn Tyr Asn Gly Tyr Leu Ile Thr Pro Glu Leu Val Leu Met Tyr Cys
225 230 235 240

Asp Val Val Glu Gly Arg Trp Asn Ile Ser Ala Cys Ala Lys Leu Asp
245 250 255

Pro Lys Leu Gln Ser Met Tyr Gln Lys Gly Asn Asn Leu Trp Glu Val
260 265 270

Ile Asp Lys Leu Phe Pro Ile Met Gly Glu Lys Thr Phe Asp Val Ile
275 280 285

Ser Leu Leu Glu Pro Leu Ala Leu Ser Leu Ile Gln Thr His Asp Pro
290 295 300

Val Lys Gln Leu Arg Gly Ala Phe Leu Asn His Val Leu Ser Glu Met
305 310 315 320

Glu Leu Ile Phe Glu Ser Arg Glu Ser Ile Lys Glu Phe Leu Ser Val
325 330 335

Asp Tyr Ile Asp Lys Ile Leu Asp Ile Phe Asn Lys Ser Thr Ile Asp
340 345 350

Glu Ile Ala Glu Ile Phe Ser Phe Phe Arg Thr Phe Gly His Pro Pro
355 360 365

Leu Glu Ala Ser Ile Ala Ala Glu Lys Val Arg Lys Tyr Met Tyr Ile
370 375 380

Gly Lys Gln Leu Lys Phe Asp Thr Ile Asn Lys Cys His Ala Ile Phe
385 390 395 400

Cys Thr Ile Ile Ile Asn Gly Tyr Arg Glu Arg His Gly Gly Gln Trp
405 410 415

Pro Pro Val Thr Leu Pro Asp His Ala His Glu Phe Ile Ile Asn Ala
420 425 430

Tyr Gly Ser Asn Ser Ala Ile Ser Tyr Glu Asn Ala Val Asp Tyr Tyr
435 440 445

Gln Ser Phe Ile Gly Ile Lys Phe Asn Lys Phe Ile Glu Pro Gln Leu
450 455 460

Asp Glu Asp Leu Thr Ile Tyr Met Lys Asp Lys Ala Leu Ser Pro Lys
465 470 475 480

Lys Ser Asn Trp Asp Thr Val Tyr Pro Ala Ser Asn Leu Leu Tyr Arg
485 490 495

Thr Asn Ala Ser Asn Glu Ser Arg Arg Leu Val Glu Val Phe Ile Ala
500 505 510

Asp Ser Lys Phe Asp Pro His Gln Ile Leu Asp Tyr Val Glu Ser Gly
515 520 525

Asp Trp Leu Asp Asp Pro Glu Phe Asn Ile Ser Tyr Ser Leu Lys Glu
530 535 540

Lys Glu Ile Lys Gln Glu Gly Arg Leu Phe Ala Lys Met Thr Tyr Lys
545 550 555 560

Met Arg Ala Thr Gln Val Leu Ser Glu Thr Leu Leu Ala Asn Asn Ile
565 570 575

Gly Lys Phe Phe Gln Glu Asn Gly Met Val Lys Gly Glu Ile Glu Leu
580 585 590

Leu Lys Arg Leu Thr Thr Ile Ser Ile Ser Gly Val Pro Arg Tyr Asn
595 600 605

Glu Val Tyr Asn Asn Ser Lys Ser His Thr Asp Asp Leu Lys Thr Tyr
610 615 620

Asn Lys Ile Ser Asn Leu Asn Leu Ser Ser Asn Gln Lys Ser Lys Lys
625 630 635 640

Phe Glu Phe Lys Ser Thr Asp Ile Tyr Asn Asp Gly Tyr Glu Thr Val
645 650 655

Ser Cys Phe Leu Thr Thr Asp Leu Lys Lys Tyr Cys Leu Asn Trp Arg
660 665 670

Tyr Glu Ser Thr Ala Leu Phe Gly Glu Thr Cys Asn Gln Ile Phe Gly
675 680 685

Leu Asn Lys Leu Phe Asn Trp Leu His Pro Arg Leu Glu Gly Ser Thr
690 695 700

Ile Tyr Val Gly Asp Pro Tyr Cys Pro Pro Ser Asp Lys Glu His Ile
705 710 715 720

Ser Leu Glu Asp His Pro Asp Ser Gly Phe Tyr Val His Asn Pro Arg
725 730 735

Gly Gly Ile Glu Gly Phe Cys Gln Lys Leu Trp Thr Leu Ile Ser Ile
740 745 750

Ser Ala Ile His Leu Ala Ala Val Arg Ile Gly Val Arg Val Thr Ala
755 760 765

Met Val Gln Gly Asp Asn Gln Ala Ile Ala Val Thr Thr Arg Val Pro
770 775 780

Asn Asn Tyr Asp Tyr Arg Val Lys Lys Glu Ile Val Tyr Lys Asp Val
785 790 795 800

Val Arg Phe Phe Asp Ser Leu Arg Glu Val Met Asp Asp Leu Gly His
805 810 815

Glu Leu Lys Leu Asn Glu Thr Ile Ile Ser Ser Lys Met Phe Ile Tyr
820 825 830

Ser Lys Arg Ile Tyr Tyr Asp Gly Arg Ile Leu Pro Gln Ala Leu Lys
835 840 845

Ala Leu Ser Arg Cys Val Phe Trp Ser Glu Thr Val Ile Asp Glu Thr
850 855 860

Arg Ser Ala Ser Ser Asn Leu Ala Thr Ser Phe Ala Lys Ala Ile Glu
865 870 875 880

Asn Gly Tyr Ser Pro Val Leu Gly Tyr Ala Cys Ser Ile Phe Lys Asn
885 890 895

Ile Gln Gln Leu Tyr Ile Ala Leu Gly Met Asn Ile Asn Pro Thr Ile
900 905 910

Thr Gln Asn Ile Arg Asp Gln Tyr Phe Arg Asn Pro Asn Trp Met Gln
915 920 925

Tyr Ala Ser Leu Ile Pro Ala Ser Val Gly Gly Phe Asn His Met Ala
930 935 940

Met Ser Arg Cys Phe Val Arg Asn Ile Gly Asp Pro Ser Val Ala Ala
945 950 955 960

Leu Ala Asp Ile Lys Arg Phe Ile Lys Ala Asn Leu Leu Asp Arg Ser
965 970 975

Val Leu Tyr Arg Ile Met Asn Gln Glu Pro Gly Glu Ser Ser Phe Phe
980 985 990

Asp Trp Ala Ser Asp Pro Tyr Ser Cys Asn Leu Pro Gln Ser Gln Asn
995 1000 1005

Ile Thr Thr Met Ile Lys Asn Ile Thr Ala Arg Asn Val Leu Gln Asp

1010 1015 1020

Ser Pro Asn Pro Leu Leu Ser Gly Leu Phe Thr Asn Thr Met Ile Glu
1025 1030 1035 1040

Glu Asp Glu Glu Leu Ala Glu Phe Leu Met Asp Arg Lys Val Ile Leu
1045 1050 1055

Pro Arg Val Ala His Asp Ile Leu Asp Asn Ser Leu Thr Gly Ile Arg
1060 1065 1070

Asn Ala Ile Ala Gly Met Leu Asp Thr Thr Lys Ser Leu Ile Arg Val
1075 1080 1085

Gly Ile Asn Arg Gly Gly Leu Thr Tyr Ser Leu Leu Arg Lys Ile Ser
1090 1095 1100

Asn Tyr Asp Leu Val Gln Tyr Glu Thr Leu Ser Arg Thr Leu Arg Leu
1105 1110 1115 1120

Ile Val Ser Asp Lys Ile Lys Tyr Glu Asp Met Cys Ser Val Asp Leu
1125 1130 1135

Ala Ile Ala Leu Arg Gln Lys Met Trp Ile His Leu Ser Gly Gly Arg
1140 1145 1150

Met Ile Ser Gly Leu Glu Thr Pro Asp Pro Leu Glu Leu Leu Ser Gly
1155 1160 1165

Val Val Ile Thr Gly Ser Glu His Cys Lys Ile Cys Tyr Ser Ser Asp
1170 1175 1180

Gly Thr Asn Pro Tyr Thr Trp Met Tyr Leu Pro Gly Asn Ile Lys Ile
1185 1190 1195 1200

Gly Ser Ala Glu Thr Gly Ile Ser Ser Leu Arg Val Pro Tyr Phe Gly
1205 1210 1215

Ser Val Thr Asp Glu Arg Ser Glu Ala Gln Leu Gly Tyr Ile Lys Asn
1220 1225 1230

Leu Ser Lys Pro Ala Lys Ala Ala Ile Arg Ile Ala Met Ile Tyr Thr
1235 1240 1245

Trp Ala Phe Gly Asn Asp Glu Ile Ser Trp Met Glu Ala Ser Gln Ile
1250 1255 1260

Ala Gln Thr Arg Ala Asn Phe Thr Leu Asp Ser Leu Lys Ile Leu Thr
1265 1270 1275 1280

Pro Val Ala Thr Ser Thr Asn Leu Ser His Arg Leu Lys Asp Thr Ala
1285 1290 1295

Thr Gln Met Lys Phe Ser Ser Thr Ser Leu Ile Arg Val Ser Arg Phe
1300 1305 1310

Ile Thr Met Ser Asn Asp Asn Met Ser Ile Lys Glu Ala Asn Glu Thr
1315 1320 1325

Lys Asp Thr Asn Leu Ile Tyr Gln Gln Ile Met Leu Thr Gly Leu Ser
1330 1335 1340

Val Phe Glu Tyr Leu Phe Arg Leu Lys Glu Thr Thr Gly His Asn Pro
1345 1350 1355 1360

Ile Val Met His Leu His Ile Glu Asp Glu Cys Cys Ile Lys Glu Ser
1365 1370 1375

Phe Asn Asp Glu His Ile Asn Pro Glu Ser Thr Leu Glu Leu Ile Arg
1380 1385 1390

Tyr Pro Glu Ser Asn Glu Phe Ile Tyr Asp Lys Asp Pro Leu Lys Asp
1395 1400 1405

Val Asp Leu Ser Lys Leu Met Val Ile Lys Asp His Ser Tyr Thr Ile
1410 1415 1420

Asp Met Asn Tyr Trp Asp Asp Thr Asp Ile Ile His Ala Ile Ser Ile
1425 1430 1435 1440

Cys Thr Ala Ile Thr Ile Ala Asp Thr Met Ser Gln Leu Asp Arg Asp
1445 1450 1455

Asn Leu Lys Glu Ile Ile Val Ile Ala Asn Asp Asp Asp Ile Asn Ser
1460 1465 1470

Leu Ile Thr Glu Phe Leu Thr Leu Asp Ile Leu Val Phe Leu Lys Thr
1475 1480 1485

Phe Gly Gly Leu Leu Val Asn Gln Phe Ala Tyr Thr Leu Tyr Ser Leu
1490 1495 1500

Lys Ile Glu Gly Arg Asp Leu Ile Trp Asp Tyr Ile Met Arg Thr Leu
1505 1510 1515 1520

Arg Asp Thr Ser His Ser Ile Leu Lys Val Leu Ser Asn Ala Leu Ser
1525 1530 1535

His Pro Lys Val Phe Lys Arg Phe Trp Asp Cys Gly Val Leu Asn Pro
1540 1545 1550

Ile Tyr Gly Pro Asn Ile Ala Ser Gln Asp Gln Ile Lys Leu Ala Leu
1555 1560 1565

Ser Ile Cys Glu Tyr Ser Leu Asp Leu Phe Met Arg Glu Trp Leu Asn
1570 1575 1580

Gly Val Ser Leu Glu Ile Tyr Ile Cys Asp Ser Asp Met Glu Val Ala
1585 1590 1595 1600

Asn Asp Arg Lys Gln Ala Phe Ile Ser Arg His Leu Ser Phe Val Cys
1605 1610 1615

Cys Leu Ala Glu Ile Ala Ser Phe Gly Pro Asn Leu Leu Asn Leu Thr
1620 1625 1630

Tyr Leu Glu Arg Leu Asp Leu Leu Lys Gln Tyr Leu Glu Leu Asn Ile
1635 1640 1645

Lys Glu Asp Pro Thr Leu Lys Tyr Val Gln Ile Ser Gly Leu Leu Ile
1650 1655 1660

Lys Ser Phe Pro Ser Thr Val Thr Tyr Val Arg Lys Thr Ala Ile Lys
1665 1670 1675 1680

Tyr Leu Arg Ile Arg Gly Ile Ser Pro Pro Glu Val Ile Asp Asp Trp
1685 1690 1695

Asp Pro Val Glu Asp Glu Asn Met Leu Asp Asn Ile Val Lys Thr Ile
1700 1705 1710

Asn Asp Asn Cys Asn Lys Asp Asn Lys Gly Asn Lys Ile Asn Asn Phe
1715 1720 1725

Trp Gly Leu Ala Leu Lys Asn Tyr Gln Val Leu Lys Ile Arg Ser Ile
1730 1735 1740

Thr Ser Asp Ser Asp Asp Asn Asp Arg Leu Asp Ala Asn Thr Ser Gly
1745 1750 1755 1760

Leu Thr Leu Pro Gln Gly Gly Asn Tyr Leu Ser His Gln Leu Arg Leu
1765 1770 1775

Phe Gly Ile Asn Ser Thr Ser Cys Leu Lys Ala Leu Glu Leu Ser Gln
1780 1785 1790

Ile Leu Met Lys Glu Val Asn Lys Asp Lys Asp Arg Leu Phe Leu Gly
1795 1800 1805

Glu Gly Ala Gly Ala Met Leu Ala Cys Tyr Asp Ala Thr Leu Gly Pro
1810 1815 1820

Ala Val Asn Tyr Tyr Asn Ser Gly Leu Asn Ile Thr Asp Val Ile Gly
1825 1830 1835 1840

Gln Arg Glu Leu Lys Ile Phe Pro Ser Glu Val Ser Leu Val Gly Lys

1845 1850 1855

Lys Leu Gly Asn Val Thr Gln Ile Leu Asn Arg Val Lys Val Leu Phe
1860 1865 1870

Asn Gly Asn Pro Asn Ser Thr Trp Ile Gly Asn Met Glu Cys Glu Ser
1875 1880 1885

Leu Ile Trp Ser Glu Leu Asn Asp Lys Ser Ile Gly Leu Val His Cys
1890 1895 1900

Asp Met Glu Gly Ala Ile Gly Lys Ser Glu Glu Thr Val Leu His Glu
1905 1910 1915 1920

His Tyr Ser Val Ile Arg Ile Thr Tyr Leu Ile Gly Asp Asp Asp Val
1925 1930 1935

Val Leu Val Ser Lys Ile Ile Pro Thr Ile Thr Pro Asn Trp Ser Arg
1940 1945 1950

Ile Leu Tyr Leu Tyr Lys Leu Tyr Trp Lys Asp Val Ser Ile Ile Ser
1955 1960 1965

Leu Lys Thr Ser Asn Pro Ala Ser Thr Glu Leu Tyr Leu Ile Ser Lys
1970 1975 1980

Asp Ala Tyr Cys Thr Ile Met Glu Pro Ser Glu Ile Val Leu Ser Lys
1985 1990 1995 2000

Leu Lys Arg Leu Ser Leu Leu Glu Glu Asn Asn Leu Leu Lys Trp Ile
2005 2010 2015

Ile Leu Ser Lys Lys Arg Asn Asn Glu Trp Leu His His Glu Ile Lys
2020 2025 2030

Glu Gly Glu Arg Asp Tyr Gly Ile Met Arg Pro Tyr His Met Ala Leu
2035 2040 2045

Gln Ile Phe Gly Phe Gln Ile Asn Leu Asn His Leu Ala Lys Glu Phe
2050 2055 2060

Leu Ser Thr Pro Asp Leu Thr Asn Ile Asn Asn Ile Ile Gln Ser Phe
2065 2070 2075 2080

Gln Arg Thr Ile Lys Asp Val Leu Phe Glu Trp Ile Asn Ile Thr His
2085 2090 2095

Asp Asp Lys Arg His Lys Leu Gly Gly Arg Tyr Asn Ile Phe Pro Leu
2100 2105 2110

Lys Asn Lys Gly Lys Leu Arg Leu Leu Ser Arg Arg Leu Val Leu Ser
2115 2120 2125

Trp Ile Ser Leu Ser Leu Ser Thr Arg Leu Leu Thr Gly Arg Phe Pro
2130 2135 2140

Asp Glu Lys Phe Glu His Arg Ala Gln Thr Gly Tyr Val Ser Leu Ala
2145 2150 2155 2160

Asp Thr Asp Leu Glu Ser Leu Lys Leu Leu Ser Lys Asn Ile Ile Lys
2165 2170 2175

Asn Tyr Arg Glu Cys Ile Gly Ser Ile Ser Tyr Trp Phe Leu Thr Lys
2180 2185 2190

Glu Val Lys Ile Leu Met Lys Leu Ile Gly Gly Ala Lys Leu Leu Gly
2195 2200 2205

Ile Pro Arg Gln Tyr Lys Glu Pro Glu Asp Gln Leu Leu Glu Asn Tyr
2210 2215 2220

Asn Gln His Asp Glu Phe Asp Ile Asp
2225 2230

(2) INFORMATION FOR SEQ ID NO:21:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 15462 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:21:

ACCAAACAAG AGAAGAAACT TGCTTGGTAA TATAAATTTA ACTTAAAATT AACTTAGGAT 60

TTAAGACATT GACTAGAAGG TCAAGAAAAG GGAACTCTAT AATTTCAAAA ATGTTGAGCC 120

TATTTGATAC ATTTAATGCA CGTAGGCAAG AAAACATAAC AAAATCAGCC GGTGGAGCTA 180

TCATTCCTGG ACAGAAAAAT ACTGTCTCTA TATTCGCCCT TGGACCGACA ATAACTGATG 240

ATAATGAGAA AATGACATTA GCTCTTCTAT TTCTATCTCA TTCACTAGAT AATGAGAAAC 300

AACATGCACA AAGGGCAGGG TTCTTGGTGT CTTTATTGTC AATGGCTTAT GCCAATCCAG 360

AGCTCTACCT AACAACAAAT GGAAGTAATG CAGATGCCAA GTATGTCATA TACATGATTG 420

AGAAAGATCT AAAACGGCAA AAGTATGGAG GATTTGTGGT TAAGACGAGA GAGATGATAT 480

ATGAAAAGAC AACTGATTGG ATATTTGGAA GTGACCTGGA TTATGATCAG GAAACTATGT 540
TGCAGAACGG CAGGAACAAT TCAACAATTG AAGACCTTGT CCACACATTT GGGTATCCAT 600
CATGTTTAGG AGCTCTTATA ATACAGATCT GGATAGTTCT GGTCAAAGCT ATCACTAGTA 660
TCTCAGGGTT AAGAAAAGGC TTTTTCACCC GATTGGAAGC TTTCAGACAA GATGGAACAG 720
TGCAGGCAGG GCTGGTATTG AGCGGTGACA CAGTGGATCA GATTGGGTCA ATCATGCGGT 780
CTCAACAGAG CTTGGTAACT CTTATGGTTG AAACATTAAT AACAATGAAT ACCAGCAGAA 840
ATGACCTCAC AACCATAGAA AAGAATATAC AAATTGTTGG CAACTACATA AGAGATGCAG 900
GTCTCGCTTC ATTCTTCAAT ACAATCAGAT ATGGAATTGA GACCAGAATG GCAGCTTTGA 960
CTCTATCCAC TCTCAGACCA GATATCAATA GATTAAAAGC TTTGATGGAA CTGTATTTAT 1020
CAAAGGGACC ACGCGCTCCT TTCATCTGTA TCCTCAGAGA TCCTATACAT GGTGAGTTCG 1080
CACCAGGCAA CTATCCTGCC ATATGGAGCT ATGCAATGGG GGTGGCAGTT GTACAAAATA 1140
GAGCCATGCA ACAGTATGTG ACGGGAAGAT CATATCTAGA CATTGATATG TTCCAGCTAG 1200
GACAAGCAGT AGCACGTGAT GCCGAAGCTC AAATGAGCTC AACACTGGAA GATGAACTTG 1260
GAGTGACACA CGAAGCTAAA GAAAGCTTGA AGAGACATAT AAGGAACATA AACAGTTCAG 1320
AGACATCTTT CCACAAACCG ACAGGTGGAT CAGCCATAGA GATGGCAATA GATGAAGAGC 1380
CAGAACAATT CGAACATAGA GCAGATCAAG AACAAAATGG AGAACCTCAA TCATCCATAA 1440
TTCAATATGC CTGGGCAGAA GGAAATAGAA GCGATGATCA GACTGAGCAA GCTACAGAAT 1500
CTGACAATAT CAAGACCGAA CAACAAAACA TCAGAGACAG ACTAAACAAG AGACTCAACG 1560
ACAAGAAGAA ACAAAGCAGT CAACCACCCA CTAATCCCAC AAACAGAACA AACCAGGACG 1620
AAATAGATGA TCTGTTTAAC GCATTTGGAA GCAACTAATC GAATCAACAT TTTAATCTAA 1680
ATCAATAATA AATAAGAAAA ACTTAGGATT AAAGAATCCT ATCATACCGG AATATAGGGT 1740
GGTAAATTTA GAGTCTGCTT GAAACTCAAT CAATAGAGAG TTGATGGAAA GCGATGCTAA 1800
AAACTATCAA ATCATGGATT CTTGGGAAGA GGAATCAAGA GATAAATCAA CTAATATCTC 1860
CTCGGCCCTC AACATCATTG AATTCATACT CAGCACCGAC CCCCAAGAAG ACTTATCGGA 1920
AAACGACACA ATCAACACAA GAACCCAGCA ACTCAGTGCC ACCATCTGTC AACCAGAAAT 1980
CAAACCAACA GAAACAAGTG AGAAAGATAG TGGATCAACT GACAAAAATA GACAGTCTGG 2040

GTCATCACAC GAATGTACAA CAGAAGCAAA AGATAGAAAC ATTGATCAGG AAACTGTACA 2100

GAGAGGACCT GGGAGAAGAA GCAGCTCAGA TAGTAGAGCT GAGACTGTGG TCTCTGGAGG 2160

AATCCCCAGA AGCATCACAG ATTCTAAAAA TGGAACCCAA AACACGGAGG ATATTGATCT 2220

CAATGAAATT AGAAAGATGG ATAAGGACTC TATTGAGGGG AAAATGCGAC AATCTGCAAA 2280

TGTTCCAAGC GAGATATCAG GAAGTGATGA CATATTTACA ACAGAACAAA GTAGAAACAG 2340

TGATCATGGA AGAAGCCTGG AATCTATCAG TACACCTGAT ACAAGATCAA TAAGTGTTGT 2400

TACTGCTGCA ACACCAGATG ATGAAGAAGA AATACTAATG AAAAATAGTA GGACAAAGAA 2460

AAGTTCTTCA ACACATCAAG AAGATGACAA AAGAATTAAA AAAGGGGGAA AAGGGAAAGA 2520

CTGGTTTAAG AAATCAAAAG ATACCGACAA CCAGATACCA ACATCAGACT ACAGATCCAC 2580

ATCAAAAGGG CAGAAGAAAA TCTCAAAGAC AACAACCACC AACACCGACA CAAAGGGGCA 2640

AACAGAAATA CAGACAGAAT CATCAGAAAC ACAATCCTCA TCATGGAATC TCATCATCGA 2700

CAACAACACC GACCGGAACG AACAGACAAG CACAACTCCT CCAACAACAA CTTCCAGATC 2760

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TATGACTGAG AGAGGAGGAA AGAAAGACCA AAATGAATCC AATGAGAGAG TATCCATGAT 3240

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CGATGTACAA GTTAAATCAG AGATATTAAG TTCATACAAT GAGTCAAATG CAACAAGACT 3420

AATACCCAAA AAAGTGAGCA GTACAATGAG ATCACTAGTT GCAGTCATCA ACAACAGCAA 3480

TCTCTCACAA AGCACAAAAC AATCATACAT AAACGAACTC AAACGTTGCA AAAATGATGA 3540

AGAAGTATCT GAATTAATGG ACATGTTCAA TGAAGATGTC AACAATTGCC AATGATCCAA 3600

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AATTATAACA CATAAAGAAT GTAGTACAGT AGGTATCAAC GGAATGCTGT TCAATACAAA 6360

TAAAGAAGGA ACTCTTGCAT TCTATACACC AAATGATATA ACACTAAACA ATTCTGTTAC 6420

ACTTGATCCA ATTGACATAT CAATCGAGCT CAACAAGGCC AAATCAGATC TAGAAGAATC 6480

AAAAGAATGG ATAAGAAGGT CAAATCAAAA ACTAGATTCT ATTGGAAATT GGCATCAATC 6540

TAGCACTACA ATCATAATTA TTTTGATAAT GATCATTATA TTGTTTATAA TTAATATAAC 6600

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TGACAAGCCA TATGTACTAA CAAACAAATA ACATATCTAC AGATCATTAG ATATTAAAAT 6720

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CCCAATAGAC AAATCCAAAT TCGAGATGGA ATACTGGAAG CATACCAATC ACGGAAAGGA 6840

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AATATACATA TTATGGACAA TAATCCTGGT GTTATTATCA ATAGTCTTCA TCATAGTGCT 6960

AATTAATTCC ATCAAAAGTG AAAAGGCCCA CGAATCATTG CTGCAAGACA TAAATAATGA 7020

GTTTATGGAA ATTACAGAAA AGATCCAAAT GGCATCGGAT AATACCAATG ATCTAATACA 7080

GTCAGGAGTG AATACAAGGC TTCTTACAAT TCAGAGTCAT GTCCAGAATT ACATACCAAT 7140

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TCCAGATGAT TTTTGGAGAT GCACGTCTGG TCTTCCATCT TTAATGAAAA CTCCAAAAAT 7320

AAGGTTAATG CCAGGGCCGG GATTATTAGC TATGCCAACG ACTGTTGATG GCTGTGTTAG 7380

AACTCCGTCT TTAGTTATAA ATGATCTGAT TTATGCTTAT ACCTCAAATC TAATTACTCG 7440

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AAAATTGAAA GTATGGACGA TATCTATGCG ACAAAATTAC TGGGGGTCAG AAGGAAGGTT 8040

ACTTCTACTA GGTAACAAGA TCTATATATA TACAAGATCT ACAAGTTGGC ATAGCAAGTT 8100

ACAATTAGGA ATAATTGATA TTACTGATTA CAGTGATATA AGGATAAAAT GGACATGGCA 8160

TAATGTGCTA TCAAGACCAG GAAACAATGA ATGTCCATGG GGACATTCAT GTCCAGATGG 8220

ATGTATAACA GGAGTATATA CTGATGCATA TCCACTCAAT CCCACAGGGA GCATTGTGTC 8280

ATCTGTCATA TTAGACTCAC AAAAATCGAG AGTGAACCCA GTCATAACTT ACTCAACAGC 8340

AACCGAAAGA GTAAACGAGC TGGCCATCCT AAACAGAACA CTCTCAGCTG GATATACAAC 8400

AACAAGCTGC ATTACACACT ATAACAAAGG ATATTGTTTT CATATAGTAG AAATAAATCA 8460

TAAAAGCTTA AACACATTTC AACCCATGTT GTTCAAAACA GAGATTCCAA AAAGCTGCAG 8520

TTAATCATAA TTAACCATAA TATGCATCAA TCTATCTATA ATACAAGTAT ATGATAAGTA 8580

ATCAGCAATC AGACAATAGA CAAAAGGGAA ATATAAAAAA CTTAGGAGCA AAGCGTGCTC 8640

GGGAAATGGA CACTGAATCT AACAATGGCA CTGTATCTGA CATACTCTAT CCTGAGTGTC 8700

ACCTTAACTC TCCTATCGTT AAAGGTAAAA TAGCACAATT ACACACTATT ATGAGTCTAC 8760

CTCAGCCTTA TGATATGGAT GACGACTCAA TACTAGTTAT CACTAGACAG AAAATAAAAC 8820

TTAATAAATT GGATAAAAGA CAACGATCTA TTAGAAGATT AAAATTAATA TTAACTGAAA 8880

AAGTGAATGA CTTAGGAAAA TACACATTTA TCAGATATCC AGAAATGTCA AAAGAAATGT 8940

TCAAATTATA TATACCTGGT ATTAACAGTA AAGTGACTGA ATTATTACTT AAAGCAGATA 9000

GAACATATAG TCAAATGACT GATGGATTAA GAGATCTATG GATTAATGTG CTATCAAAAT 9060

TAGCCTCAAA AAATGATGGA AGCAATTATG ATCTTAATGA AGAAATTAAT AATATATCGA 9120

AAGTTCACAC AACCTATAAA TCAGATAAAT GGTATAATCC ATTCAAAACA TGGTTTACTA 9180

TCAAGTATGA TATGAGAAGA TTACAAAAAG CTCGAAATGA GATCACTTTT AATGTTGGGA 9240

AGGATTATAA CTTGTTAGAA GACCAGAAGA ATTTCTTATT GATACATCCA GAATTGGTTT 9300

TGATATTAGA TAAACAAAAC TACAATGGTT ATCTAATTAC TCCTGAATTA GTATTGATGT 9360

ATTGTGACGT AGTCGAAGGC CGATGGAATA TAAGTGCATG TGCTAAGTTA GATCCAAAAT 9420

TACAATCTAT GTATCAGAAA GGTAATAACC TGTGGGAAGT GATAGATAAA TTGTTTCCAA 9480

TTATGGGAGA AAAGACATTT GATGTGATAT CGTTATTAGA ACCACTTGCA TTATCCTTAA 9540

TTCAAACTCA TGATCCTGTT AAACAACTAA GAGGAGCTTT TTTAAATCAT GTGTTATCCG 9600

AGATGGAATT AATATTTGAA TCTAGAGAAT CGATTAAGGA ATTTCTGAGT GTAGATTACA 9660

TTGATAAAAT TTTAGATATA TTTAATAAGT CTACAATAGA TGAAATAGCA GAGATTTTCT 9720

CTTTTTTTAG AACATTTGGG CATCCTCCAT TAGAAGCTAG TATTGCAGCA GAAAAGGTTA 9780

GAAAATATAT GTATATTGGA AAACAATTAA AATTTGACAC TATTAATAAA TGTCATGCTA 9840

TCTTCTGTAC AATAATAATT AACGGATATA GAGAGAGGCA TGGTGGACAG TGGCCTCCTG 9900

TGACATTACC TGATCATGCA CACGAATTCA TCATAAATGC TTACGGTTCA AACTCTGCGA 9960

TATCATATGA GAATGCTGTT GATTATTACC AGAGCTTTAT AGGAATAAAA TTCAATAAAT 10020

TCATAGAGCC TCAGTTAGAT GAGGATTTGA CAATTTATAT GAAAGATAAA GCATTATCTC 10080

CAAAAAAATC AAATTGGGAC ACAGTTTATC CTGCATCTAA TTTACTGTAC CGTACTAACG 10140

CATCCAACGA ATCACGAAGA TTAGTTGAAG TATTTATAGC AGATAGTAAA TTTGATCCTC 10200

ATCAGATATT GGATTATGTA GAATCTGGGG ACTGGTTAGA TGATCCAGAA TTTAATATTT 10260

CTTATAGTCT TAAAGAAAAA GAGATCAAAC AGGAAGGTAG ACTCTTTGCA AAAATGACAT 10320

ACAAAATGAG AGCTACACAA GTTTTATCAG AGACACTACT TGCAAATAAC ATAGGAAAAT 10380

TCTTTCAAGA AAATGGGATG GTGAAGGGAG AGATTGAATT ACTTAAGAGA TTAACAACCA 10440

TATCAATATC AGGAGTTCCA CGGTATAATG AAGTGTACAA TAATTCTAAA AGCCATACAG 10500

ATGACCTTAA AACCTACAAT AAAATAAGTA ATCTTAATTT GTCTTCTAAT CAGAAATCAA 10560

AGAAATTTGA ATTCAAGTCA ACGGATATCT ACAATGATGG ATACGAGACT GTGAGCTGTT 10620

TCCTAACAAC AGATCTCAAA AAATACTGTC TTAATTGGAG ATATGAATCA ACAGCTCTAT 10680

TTGGAGAAAC TTGCAACCAA ATATTTGGAT TAAATAAATT GTTTAATTGG TTACACCCTC 10740

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ATATATCATT AGAGGATCAC CCTGATTCTG GTTTTTACGT TCATAACCCA AGAGGGGGTA 10860

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CTGTTAGAAT AGGCGTGAGG GTGACTGCAA TGGTTCAAGG AGACAATCAA GCTATAGCTG 10980

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ATGTAGTGAG ATTTTTTGAT TCATTAAGAG AAGTGATGGA TGATCTAGGT CATGAACTTA 11100

AATTAAATGA AACGATTATA AGTAGCAAGA TGTTCATATA TAGCAAAAGA ATCTATTATG 11160

ATGGGAGAAT TCTTCCTCAA GCTCTAAAAG CATTATCTAG ATGTGTCTTC TGGTCAGAGA 11220

CAGTAATAGA CGAAACAAGA TCAGCATCTT CAAATTTGGC AACATCATTT GCAAAAGCAA 11280

TTGAGAATGG TTATTCACCT GTTCTAGGAT ATGCATGCTC AATTTTTAAG AACATTCAAC 11340

AACTATATAT TGCCCTTGGG ATGAATATCA ATCCAACTAT AACACAGAAT ATCAGAGATC 11400

AGTATTTTAG GAATCCAAAT TGGATGCAAT ATGCCTCTTT AATACCTGCT AGTGTTGGGG 11460

GATTCAATCA CATGGCCATG TCAAGATGTT TTGTAAGGAA TATTGGTGAT CCATCAGTTG 11520

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ATTCATGCAA TTTACCACAA TCTCAAAATA TAACCACCAT GATAAAAAAT ATAACAGCAA 11700

GGAATGTATT ACAAGATTCA CCAAATCCAT TATTATCTGG ATTATTCACA AATACAATGA 11760

TAGAAGAAGA TGAAGAATTA GCTGAGTTCC TGATGGACAG GAAGGTAATT CTCCCTAGAG 11820

TTGCACATGA TATTCTAGAT AATTCTCTCA CAGGAATTAG AAATGCCATA GCTGGAATGT 11880

TAGATACGAC AAAATCACTA ATTCGGGTTG GCATAAATAG AGGAGGACTG ACATATAGTT 11940

TGTTGAGGAA AATCAGTAAT TACGATCTAG TACAATATGA AACACTAAGT AGGACTTTGC 12000

GACTAATTGT AAGTGATAAA ATCAAGTATG AAGATATGTG TTCGGTAGAC CTTGCCATAG 12060

CATTGCGACA AAAGATGTGG ATTCATTTAT CAGGAGGAAG GATGATAAGT GGACTTGAAA 12120

CGCCTGACCC ATTAGAATTA CTATCTGGGG TAGTAATAAC AGGATCAGAA CATTGTAAAA 12180

TATGTTATTC TTCAGATGGC ACAAACCCAT ATACTTGGAT GTATTTACCC GGTAATATCA 12240

AAATAGGATC AGCAGAAACA GGTATATCGT CATTAAGAGT TCCTTATTTT GGATCAGTCA 12300

CTGATGAAAG ATCTGAAGCA CAATTAGGAT ATATCAAGAA TCTTAGTAAA CCTGCAAAAG 12360

CCGCAATAAG AATAGCAATG ATATATACAT GGGCATTTGG TAATGATGAG ATATCTTGGA 12420

TGGAAGCCTC ACAGATAGCA CAAACACGTG CAAATTTTAC ACTAGATAGT CTCAAAATTT 12480

TAACACCGGT AGCTACATCA ACAAATTTAT CACACAGATT TAAGGATACT GCAACTCAGA 12540

TGAAATTCTC CAGTACATCA TTGATCAGAG TCAGCAGATT TATAACAATG TCCAATGATA 12600

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TGTTAACAGG ATTAAGTGTT TTCGAATATT TATTTAGATT AAAAGAAACC ACAGGACACA 12720

ACCCTATAGT TATGCATCTG CACATAGAAG ATGAGTGTTG TATTAAAGAA AGTTTTAATG 12780

ATGAACATAT TAATCCAGAG TCTACATTAG AATTAATTCG ATATCCTGAA AGTAATGAAT 12840

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ACCATTCTTA CACAATTGAT ATGAATTATT GGGATGATAC TGACATCATA CATGCAATTT 12960

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AAGAGATAAT AGTTATTGCA AATGATGATG ATATTAATAG CTTAATCACT GAATTTTTGA 13080

CTCTTGACAT ACTTGTATTT CTCAAGACAT TTGGTGGATT ATTAGTAAAT CAATTTGCAT 13140

ACACTCTTTA TAGTCTAAAA ATAGAAGGTA GGGATCTCAT TTGGGATTAT ATAATGAGAA 13200

CACTGAGAGA TACTTCCCAT TCAATATTAA AAGTATTATC TAATGCATTA TCTCATCCTA 13260

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TGAGAGAATG GTTGAATGGT GTATCACTTG AAATATACAT TTGTGACAGC GATATGGAAG 13440

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TATTGAAACA ATATCTTGAA TTAAATATTA AAGAAGACCC TACTCTTAAA TATGTACAAA 13620

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TCAAATATCT AAGGATTCGC GGTATTAGTC CACCTGAGGT AATTGATGAT TGGGATCCGG 13740

TAGAAGATGA AAATATGCTG GATAACATTG TCAAAACTAT AAATGATAAC TGTAATAAAG 13800

ATAATAAAGG GAATAAAATT AACAATTTCT GGGGACTAGC ACTTAAGAAC TATCAAGTCC 13860

TTAAAATCAG ATCTATAACA AGTGATTCTG ATGATAATGA TAGACTAGAT GCTAATACAA 13920

GTGGTTTGAC ACTTCCTCAA GGAGGGAATT ATCTATCGCA TCAATTGAGA TTATTCGGAA 13980

TCAACAGCAC TAGTTGTCTG AAAGCTCTTG AGTTATCACA AATTTTAATG AAGGAAGTCA 14040

ATAAAGACAA GGACAGGCTC TTCCTGGGAG AAGGAGCAGG AGCTATGCTA GCATGTTATG 14100

ATGCCACATT AGGACCTGCA GTTAATTATT ATAATTCAGG TTTGAATATA ACAGATGTAA 14160

TTGGTCAACG AGAATTGAAA ATATTTCCTT CAGAGGTATC ATTAGTAGGT AAAAAATTAG 14220

GAAATGTGAC ACAGATTCTT AACAGGGTAA AAGTACTGTT CAATGGGAAT CCTAATTCAA 14280

CATGGATAGG AAATATGGAA TGTGAGAGCT TAATATGGAG TGAATTAAAT GATAAGTCCA 14340

TTGGATTAGT ACATTGTGAT ATGGAAGGAG CTATCGGTAA ATCAGAAGAA ACTGTTCTAC 14400

ATGAACATTA TAGTGTTATA AGAATTACAT ACTTGATTGG GGATGATGAT GTTGTTTTAG 14460

TTTCCAAAAT TATACCTACA ATCACTCCGA ATTGGTCTAG AATACTTTAT CTATATAAAT 14520

TATATTGGAA AGATGTAAGT ATAATATCAC TCAAAACTTC TAATCCTGCA TCAACAGAAT 14580

TATATCTAAT TTCGAAAGAT GCATATTGTA CTATAATGGA ACCTAGTGAA ATTGTTTTAT 14640

CAAAACTTAA AAGATTGTCA CTCTTGGAAG AAAATAATCT ATTAAAATGG ATCATTTTAT 14700

CAAAGAAGAG GAATAATGAA TGGTTACATC ATGAAATCAA AGAAGGAGAA AGAGATTATG 14760

GAATCATGAG ACCATATCAT ATGGCACTAC AAATCTTTGG ATTTCAAATC AATTTAAATC 14820

ATCTGGCGAA AGAATTTTTA TCAACCCCAG ATCTGACTAA TATCAACAAT ATAATCCAAA 14880

GTTTTCAGCG AACAATAAAG GATGTTTTAT TTGAATGGAT TAATATAACT CATGATGATA 14940

AGAGACATAA ATTAGGCGGA AGATATAACA TATTCCCACT GAAAAATAAG GGAAAGTTAA 15000

GACTGCTATC GAGAAGACTA GTATTAAGTT GGATTTCATT ATCATTATCG ACTCGATTAC 15060

TTACAGGTCG CTTTCCTGAT GAAAAATTTG AACATAGAGC ACAGACTGGA TATGTATCAT 15120

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GAGAGTGTAT AGGATCAATA TCATATTGGT TTCTAACCAA AGAAGTTAAA ATACTTATGA 15240

AATTGATTGG TGGTGCTAAA TTATTAGGAA TTCCCAGACA ATATAAAGAA CCCGAAGACC 15300

AGTTATTAGA AAACTACAAT CAACATGATG AATTTGATAT CGATTAAAAC ATAAATACAA 15360

TGAAGATATA TCCTAACCTT TATCTTTAAG CCTAGGAATA GACAAAAAGT AAGAAAAACA 15420

TGTAATATAT ATATACCAAA CAGAGTTCTT CTCTTGTTTG GT 15462

(2) INFORMATION FOR SEQ ID NO:22:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2233 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

Met Asp Thr Glu Ser Asn Asn Gly Thr Val Ser Asp Ile Leu Tyr Pro
1 5 10 15

Glu Cys His Leu Asn Ser Pro Ile Val Lys Gly Lys Ile Ala Gln Leu

20 25 30

His Thr Ile Met Ser Leu Pro Gln Pro Tyr Asp Met Asp Asp Asp Ser
35 40 45

Ile Leu Val Ile Thr Arg Gln Lys Ile Lys Leu Asn Lys Leu Asp Lys
50 55 60

Arg Gln Arg Ser Ile Arg Arg Leu Lys Leu Ile Leu Thr Glu Lys Val
65 70 75 80

Asn Asp Leu Gly Lys Tyr Thr Phe Ile Arg Tyr Pro Glu Met Ser Lys
85 90 95

Glu Met Phe Lys Leu Tyr Ile Pro Gly Ile Asn Ser Lys Val Thr Glu
100 105 110

Leu Leu Leu Lys Ala Asp Arg Thr Tyr Ser Gln Met Thr Asp Gly Leu
115 120 125

Arg Asp Leu Trp Ile Asn Val Leu Ser Lys Leu Ala Ser Lys Asn Asp
130 135 140

Gly Ser Asn Tyr Asp Leu Asn Glu Glu Ile Asn Asn Ile Ser Lys Val
145 150 155 160

His Thr Thr Tyr Lys Ser Asp Lys Trp Tyr Asn Pro Phe Lys Thr Trp
165 170 175

Phe Thr Ile Lys Tyr Asp Met Arg Arg Leu Gln Lys Ala Arg Asn Glu
180 185 190

Ile Thr Phe Asn Val Gly Lys Asp Tyr Asn Leu Leu Glu Asp Gln Lys
195 200 205

Asn Phe Leu Leu Ile His Pro Glu Leu Val Leu Ile Leu Asp Lys Gln
210 215 220

Asn Tyr Asn Gly Tyr Leu Ile Thr Pro Glu Leu Val Leu Met Tyr Cys
225 230 235 240

Asp Val Val Glu Gly Arg Trp Asn Ile Ser Ala Cys Ala Lys Leu Asp
245 250 255

Pro Lys Leu Gln Ser Met Tyr Gln Lys Gly Asn Asn Leu Trp Glu Val
260 265 270

Ile Asp Lys Leu Phe Pro Ile Met Gly Glu Lys Thr Phe Asp Val Ile
275 280 285

Ser Leu Leu Glu Pro Leu Ala Leu Ser Leu Ile Gln Thr His Asp Pro
290 295 300

Val Lys Gln Leu Arg Gly Ala Phe Leu Asn His Val Leu Ser Glu Met
305 310 315 320

Glu Leu Ile Phe Glu Ser Arg Glu Ser Ile Lys Glu Phe Leu Ser Val
325 330 335

Asp Tyr Ile Asp Lys Ile Leu Asp Ile Phe Asn Lys Ser Thr Ile Asp
340 345 350

Glu Ile Ala Glu Ile Phe Ser Phe Phe Arg Thr Phe Gly His Pro Pro
355 360 365

Leu Glu Ala Ser Ile Ala Ala Glu Lys Val Arg Lys Tyr Met Tyr Ile
370 375 380

Gly Lys Gln Leu Lys Phe Asp Thr Ile Asn Lys Cys His Ala Ile Phe
385 390 395 400

Cys Thr Ile Ile Ile Asn Gly Tyr Arg Glu Arg His Gly Gly Gln Trp
405 410 415

Pro Pro Val Thr Leu Pro Asp His Ala His Glu Phe Ile Ile Asn Ala
420 425 430

Tyr Gly Ser Asn Ser Ala Ile Ser Tyr Glu Asn Ala Val Asp Tyr Tyr
435 440 445

Gln Ser Phe Ile Gly Ile Lys Phe Asn Lys Phe Ile Glu Pro Gln Leu
450 455 460

Asp Glu Asp Leu Thr Ile Tyr Met Lys Asp Lys Ala Leu Ser Pro Lys
465 470 475 480

Lys Ser Asn Trp Asp Thr Val Tyr Pro Ala Ser Asn Leu Leu Tyr Arg
485 490 495

Thr Asn Ala Ser Asn Glu Ser Arg Arg Leu Val Glu Val Phe Ile Ala
500 505 510

Asp Ser Lys Phe Asp Pro His Gln Ile Leu Asp Tyr Val Glu Ser Gly
515 520 525

Asp Trp Leu Asp Asp Pro Glu Phe Asn Ile Ser Tyr Ser Leu Lys Glu
530 535 540

Lys Glu Ile Lys Gln Glu Gly Arg Leu Phe Ala Lys Met Thr Tyr Lys
545 550 555 560

Met Arg Ala Thr Gln Val Leu Ser Glu Thr Leu Leu Ala Asn Asn Ile
565 570 575

Gly Lys Phe Phe Gln Glu Asn Gly Met Val Lys Gly Glu Ile Glu Leu
580 585 590

Leu Lys Arg Leu Thr Thr Ile Ser Ile Ser Gly Val Pro Arg Tyr Asn
595 600 605

Glu Val Tyr Asn Asn Ser Lys Ser His Thr Asp Asp Leu Lys Thr Tyr
610 615 620

Asn Lys Ile Ser Asn Leu Asn Leu Ser Ser Asn Gln Lys Ser Lys Lys
625 630 635 640

Phe Glu Phe Lys Ser Thr Asp Ile Tyr Asn Asp Gly Tyr Glu Thr Val
645 650 655

Ser Cys Phe Leu Thr Thr Asp Leu Lys Lys Tyr Cys Leu Asn Trp Arg
660 665 670

Tyr Glu Ser Thr Ala Leu Phe Gly Glu Thr Cys Asn Gln Ile Phe Gly
675 680 685

Leu Asn Lys Leu Phe Asn Trp Leu His Pro Arg Leu Glu Gly Ser Thr
690 695 700

Ile Tyr Val Gly Asp Pro Tyr Cys Pro Pro Ser Asp Lys Glu His Ile
705 710 715 720

Ser Leu Glu Asp His Pro Asp Ser Gly Phe Tyr Val His Asn Pro Arg
725 730 735

Gly Gly Ile Glu Gly Phe Cys Gln Lys Leu Trp Thr Leu Ile Ser Ile
740 745 750

Ser Ala Ile His Leu Ala Ala Val Arg Ile Gly Val Arg Val Thr Ala
755 760 765

Met Val Gln Gly Asp Asn Gln Ala Ile Ala Val Thr Thr Arg Val Pro
770 775 780

Asn Asn Tyr Asp Tyr Arg Val Lys Lys Glu Ile Val Tyr Lys Asp Val
785 790 795 800

Val Arg Phe Phe Asp Ser Leu Arg Glu Val Met Asp Asp Leu Gly His
805 810 815

Glu Leu Lys Leu Asn Glu Thr Ile Ile Ser Ser Lys Met Phe Ile Tyr
820 825 830

Ser Lys Arg Ile Tyr Tyr Asp Gly Arg Ile Leu Pro Gln Ala Leu Lys
835 840 845

Ala Leu Ser Arg Cys Val Phe Trp Ser Glu Thr Val Ile Asp Glu Thr

850 855 860

Arg Ser Ala Ser Ser Asn Leu Ala Thr Ser Phe Ala Lys Ala Ile Glu
865 870 875 880

Asn Gly Tyr Ser Pro Val Leu Gly Tyr Ala Cys Ser Ile Phe Lys Asn
885 890 895

Ile Gln Gln Leu Tyr Ile Ala Leu Gly Met Asn Ile Asn Pro Thr Ile
900 905 910

Thr Gln Asn Ile Arg Asp Gln Tyr Phe Arg Asn Pro Asn Trp Met Gln
915 920 925

Tyr Ala Ser Leu Ile Pro Ala Ser Val Gly Gly Phe Asn His Met Ala
930 935 940

Met Ser Arg Cys Phe Val Arg Asn Ile Gly Asp Pro Ser Val Ala Ala
945 950 955 960

Leu Ala Asp Ile Lys Arg Phe Ile Lys Ala Asn Leu Leu Asp Arg Ser
965 970 975

Val Leu Tyr Arg Ile Met Asn Gln Glu Pro Gly Glu Ser Ser Phe Phe
980 985 990

Asp Trp Ala Ser Asp Pro Tyr Ser Cys Asn Leu Pro Gln Ser Gln Asn
995 1000 1005

Ile Thr Thr Met Ile Lys Asn Ile Thr Ala Arg Asn Val Leu Gln Asp
1010 1015 1020

Ser Pro Asn Pro Leu Leu Ser Gly Leu Phe Thr Asn Thr Met Ile Glu
1025 1030 1035 1040

Glu Asp Glu Glu Leu Ala Glu Phe Leu Met Asp Arg Lys Val Ile Leu
1045 1050 1055

Pro Arg Val Ala His Asp Ile Leu Asp Asn Ser Leu Thr Gly Ile Arg
1060 1065 1070

Asn Ala Ile Ala Gly Met Leu Asp Thr Thr Lys Ser Leu Ile Arg Val
1075 1080 1085

Gly Ile Asn Arg Gly Gly Leu Thr Tyr Ser Leu Leu Arg Lys Ile Ser
1090 1095 1100

Asn Tyr Asp Leu Val Gln Tyr Glu Thr Leu Ser Arg Thr Leu Arg Leu
1105 1110 1115 1120

Ile Val Ser Asp Lys Ile Lys Tyr Glu Asp Met Cys Ser Val Asp Leu
1125 1130 1135

Ala Ile Ala Leu Arg Gln Lys Met Trp Ile His Leu Ser Gly Gly Arg
1140 1145 1150

Met Ile Ser Gly Leu Glu Thr Pro Asp Pro Leu Glu Leu Leu Ser Gly
1155 1160 1165

Val Val Ile Thr Gly Ser Glu His Cys Lys Ile Cys Tyr Ser Ser Asp
1170 1175 1180

Gly Thr Asn Pro Tyr Thr Trp Met Tyr Leu Pro Gly Asn Ile Lys Ile
1185 1190 1195 1200

Gly Ser Ala Glu Thr Gly Ile Ser Ser Leu Arg Val Pro Tyr Phe Gly
1205 1210 1215

Ser Val Thr Asp Glu Arg Ser Glu Ala Gln Leu Gly Tyr Ile Lys Asn
1220 1225 1230

Leu Ser Lys Pro Ala Lys Ala Ala Ile Arg Ile Ala Met Ile Tyr Thr
1235 1240 1245

Trp Ala Phe Gly Asn Asp Glu Ile Ser Trp Met Glu Ala Ser Gln Ile
1250 1255 1260

Ala Gln Thr Arg Ala Asn Phe Thr Leu Asp Ser Leu Lys Ile Leu Thr
1265 1270 1275 1280

Pro Val Ala Thr Ser Thr Asn Leu Ser His Arg Phe Lys Asp Thr Ala
1285 1290 1295

Thr Gln Met Lys Phe Ser Ser Thr Ser Leu Ile Arg Val Ser Arg Phe
1300 1305 1310

Ile Thr Met Ser Asn Asp Asn Met Ser Ile Lys Glu Ala Asn Glu Thr
1315 1320 1325

Lys Asp Thr Asn Leu Ile Tyr Gln Gln Ile Met Leu Thr Gly Leu Ser
1330 1335 1340

Val Phe Glu Tyr Leu Phe Arg Leu Lys Glu Thr Thr Gly His Asn Pro
1345 1350 1355 1360

Ile Val Met His Leu His Ile Glu Asp Glu Cys Cys Ile Lys Glu Ser
1365 1370 1375

Phe Asn Asp Glu His Ile Asn Pro Glu Ser Thr Leu Glu Leu Ile Arg
1380 1385 1390

Tyr Pro Glu Ser Asn Glu Phe Ile Tyr Asp Lys Asp Pro Leu Lys Asp
1395 1400 1405

Val Asp Leu Ser Lys Leu Met Val Ile Lys Asp His Ser Tyr Thr Ile
1410 1415 1420

Asp Met Asn Tyr Trp Asp Asp Thr Asp Ile Ile His Ala Ile Ser Ile
1425 1430 1435 1440

Cys Thr Ala Ile Thr Ile Ala Asp Thr Met Ser Gln Leu Asp Arg Asp
1445 1450 1455

Asn Leu Lys Glu Ile Ile Val Ile Ala Asn Asp Asp Asp Ile Asn Ser
1460 1465 1470

Leu Ile Thr Glu Phe Leu Thr Leu Asp Ile Leu Val Phe Leu Lys Thr
1475 1480 1485

Phe Gly Gly Leu Leu Val Asn Gln Phe Ala Tyr Thr Leu Tyr Ser Leu
1490 1495 1500

Lys Ile Glu Gly Arg Asp Leu Ile Trp Asp Tyr Ile Met Arg Thr Leu
1505 1510 1515 1520

Arg Asp Thr Ser His Ser Ile Leu Lys Val Leu Ser Asn Ala Leu Ser
1525 1530 1535

His Pro Lys Val Phe Lys Arg Phe Trp Asp Cys Gly Val Leu Asn Pro
1540 1545 1550

Ile Tyr Gly Pro Asn Ile Ala Ser Gln Asp Gln Ile Lys Leu Ala Leu
1555 1560 1565

Ser Ile Cys Glu Tyr Ser Leu Asp Leu Phe Met Arg Glu Trp Leu Asn
1570 1575 1580

Gly Val Ser Leu Glu Ile Tyr Ile Cys Asp Ser Asp Met Glu Val Ala
1585 1590 1595 1600

Asn Asp Arg Lys Gln Ala Phe Ile Ser Arg His Leu Ser Phe Val Cys
1605 1610 1615

Cys Leu Ala Glu Ile Ala Ser Phe Gly Pro Asn Leu Leu Asn Leu Thr
1620 1625 1630

Tyr Leu Glu Arg Leu Asp Leu Leu Lys Gln Tyr Leu Glu Leu Asn Ile
1635 1640 1645

Lys Glu Asp Pro Thr Leu Lys Tyr Val Gln Ile Ser Gly Leu Leu Ile
1650 1655 1660

Lys Ser Phe Pro Ser Thr Val Thr Tyr Val Arg Lys Thr Ala Ile Lys
1665 1670 1675 1680

Tyr Leu Arg Ile Arg Gly Ile Ser Pro Pro Glu Val Ile Asp Asp Trp

1685 1690 1695

Asp Pro Val Glu Asp Glu Asn Met Leu Asp Asn Ile Val Lys Thr Ile
1700 1705 1710

Asn Asp Asn Cys Asn Lys Asp Asn Lys Gly Asn Lys Ile Asn Asn Phe
1715 1720 1725

Trp Gly Leu Ala Leu Lys Asn Tyr Gln Val Leu Lys Ile Arg Ser Ile
1730 1735 1740

Thr Ser Asp Ser Asp Asp Asn Asp Arg Leu Asp Ala Asn Thr Ser Gly
1745 1750 1755 1760

Leu Thr Leu Pro Gln Gly Gly Asn Tyr Leu Ser His Gln Leu Arg Leu
1765 1770 1775

Phe Gly Ile Asn Ser Thr Ser Cys Leu Lys Ala Leu Glu Leu Ser Gln
1780 1785 1790

Ile Leu Met Lys Glu Val Asn Lys Asp Lys Asp Arg Leu Phe Leu Gly
1795 1800 1805

Glu Gly Ala Gly Ala Met Leu Ala Cys Tyr Asp Ala Thr Leu Gly Pro
1810 1815 1820

Ala Val Asn Tyr Tyr Asn Ser Gly Leu Asn Ile Thr Asp Val Ile Gly
1825 1830 1835 1840

Gln Arg Glu Leu Lys Ile Phe Pro Ser Glu Val Ser Leu Val Gly Lys
1845 1850 1855

Lys Leu Gly Asn Val Thr Gln Ile Leu Asn Arg Val Lys Val Leu Phe
1860 1865 1870

Asn Gly Asn Pro Asn Ser Thr Trp Ile Gly Asn Met Glu Cys Glu Ser
1875 1880 1885

Leu Ile Trp Ser Glu Leu Asn Asp Lys Ser Ile Gly Leu Val His Cys
1890 1895 1900

Asp Met Glu Gly Ala Ile Gly Lys Ser Glu Glu Thr Val Leu His Glu
1905 1910 1915 1920

His Tyr Ser Val Ile Arg Ile Thr Tyr Leu Ile Gly Asp Asp Asp Val
1925 1930 1935

Val Leu Val Ser Lys Ile Ile Pro Thr Ile Thr Pro Asn Trp Ser Arg
1940 1945 1950

Ile Leu Tyr Leu Tyr Lys Leu Tyr Trp Lys Asp Val Ser Ile Ile Ser
1955 1960 1965

Leu Lys Thr Ser Asn Pro Ala Ser Thr Glu Leu Tyr Leu Ile Ser Lys
1970 1975 1980

Asp Ala Tyr Cys Thr Ile Met Glu Pro Ser Glu Ile Val Leu Ser Lys
1985 1990 1995 2000

Leu Lys Arg Leu Ser Leu Leu Glu Glu Asn Asn Leu Leu Lys Trp Ile
2005 2010 2015

Ile Leu Ser Lys Lys Arg Asn Asn Glu Trp Leu His His Glu Ile Lys
2020 2025 2030

Glu Gly Glu Arg Asp Tyr Gly Ile Met Arg Pro Tyr His Met Ala Leu
2035 2040 2045

Gln Ile Phe Gly Phe Gln Ile Asn Leu Asn His Leu Ala Lys Glu Phe
2050 2055 2060

Leu Ser Thr Pro Asp Leu Thr Asn Ile Asn Asn Ile Ile Gln Ser Phe
2065 2070 2075 2080

Gln Arg Thr Ile Lys Asp Val Leu Phe Glu Trp Ile Asn Ile Thr His
2085 2090 2095

Asp Asp Lys Arg His Lys Leu Gly Gly Arg Tyr Asn Ile Phe Pro Leu
2100 2105 2110

Lys Asn Lys Gly Lys Leu Arg Leu Leu Ser Arg Arg Leu Val Leu Ser
2115 2120 2125

Trp Ile Ser Leu Ser Leu Ser Thr Arg Leu Leu Thr Gly Arg Phe Pro
2130 2135 2140

Asp Glu Lys Phe Glu His Arg Ala Gln Thr Gly Tyr Val Ser Leu Ala
2145 2150 2155 2160

Asp Thr Asp Leu Glu Ser Leu Lys Leu Leu Ser Lys Asn Ile Ile Lys
2165 2170 2175

Asn Tyr Arg Glu Cys Ile Gly Ser Ile Ser Tyr Trp Phe Leu Thr Lys
2180 2185 2190

Glu Val Lys Ile Leu Met Lys Leu Ile Gly Gly Ala Lys Leu Leu Gly
2195 2200 2205

Ile Pro Arg Gln Tyr Lys Glu Pro Glu Asp Gln Leu Leu Glu Asn Tyr
2210 2215 2220

Asn Gln His Asp Glu Phe Asp Ile Asp
2225 2230

(2) INFORMATION FOR SEQ ID NO:23:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 15218 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

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CAAAATCTAA CCAACTTTAC ACCACCACTT CACATCAGAC ATCTTTAGTA AGGAATAGTG 13920
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CCACAGGATG CAAGATCAGT ATAGAGTATA TTTTAAAAGA TCTTAAGATT AAGGACCCCA 14040
GTTGTATAGC ATTCATAGGT GAAGGAGCTG GTAACTTATT ATTACGTACG GTAGTAGAAC 14100
TTCATCCAGA CATAAGATAC ATTTACAGAA GTTTAAAAGA TTGCAATGAT CATAGTTTAC 14160
CTATTGAATT TCTAAGGTTA TACAACGGGC ATATAAACAT AGATTATGGT GAGAATTTAA 14220
CCATTCCTGC TACAGATGCA ACTAATAACA TTCATTGGTC TTATTTACAT ATAAAATTTG 14280
CAGAACCTAT TAGCATCTTT GTCTGCGATG CTGAATTACC TGTTACAGCC AATTGGAGTA 14340
AAATTATAAT TGAATGGAGT AAGCATGTAA GAAAGTGCAA GTACTGTTCT TCTGTAAATA 14400
GATGCATTTT AATTGCAAAA TATCATGCTC AAGATGACAT TGATTTCAAA TTAGATAACA 14460
TTACTATATT AAAAACTTAC GTGTGCCTAG GTAGCAAGTT AAAAGGATCT GAAGTTTACT 14520
TAATCCTTAC AATAGGCCCT GCAAATATAC TTCCTGTTTT TGATGTTGTA CAAAATGCTA 14580
AATTGACACT TTCAAGAACT AAAAATTTCA TTATGCCTAA AAAAACTGAC AAGGAATCTA 14640
TCGATGCAAA TATTAAAAGC TTAATACCTT TCCTTTGTTA CCCTATAACA AAAAAAGGAA 14700
TTAAGACTTC ATTGTCAAAA TTGAAGAGTG TAGTTAATGG AGATATATTA TCATATTCTA 14760
TAGCTGGACG TAATGAAGTA TTCAGCAACA AGCTTATAAA CCACAAGCAT ATGAATATCC 14820
TAAAATGGCT AGATCATGTT TTAAATTTTA GATCAGCTGA ACTTAATTAC AATCATTTAT 14880
ACATGATAGA GTCCACATAT CCTTACTTAA GTGAATTGTT AAATAGTTTA ACAACCAATG 14940
AGCTCAAGAA GCTGATTAAA ATAACAGGTA GTGTGCTATA CAACCTTCCC AACGAACAGT 15000
AGTTTAAAAT ATCATTAACA AGTTTGGTCA AATTTAGATG CTAACACATC ATTATATTAT 15060
AGTTATTAAA AAATATACAA ACTTTTCAAT AATTTAGCAT ATTGATTCCA AAATTATCAT 15120
TTTAGTCTTA AGGGGTTAAA TAAAAGTCTA AAACTAACAA TTATACATGT GCATTCACAA 15180

CACAACGAGA CATTAGTTTT TGACACTTTT TTTCTCGT 15218

(2) INFORMATION FOR SEQ ID NO:24:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2166 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:24:

Met Asp Pro Ile Ile Asn Gly Asn Ser Ala Asn Val Tyr Leu Thr Asp
1 5 10 15

Ser Tyr Leu Lys Gly Val Ile Ser Phe Ser Glu Cys Asn Ala Leu Gly
20 25 30

Ser Tyr Leu Phe Asn Gly Pro Tyr Leu Lys Asn Asp Tyr Thr Asn Leu
35 40 45

Ile Ser Arg Gln Ser Pro Leu Leu Glu His Met Asn Leu Lys Lys Leu
50 55 60

Thr Ile Thr Gln Ser Leu Ile Ser Arg Tyr His Lys Gly Glu Leu Lys
65 70 75 80

Leu Glu Glu Pro Thr Tyr Phe Gln Ser Leu Leu Met Thr Tyr Lys Ser
85 90 95

Met Ser Ser Ser Glu Gln Ile Ala Thr Thr Asn Leu Leu Lys Lys Ile
100 105 110

Ile Arg Arg Ala Ile Glu Ile Ser Asp Val Lys Val Tyr Ala Ile Leu
115 120 125

Asn Lys Leu Gly Leu Lys Glu Lys Asp Arg Val Lys Pro Asn Asn Asn
130 135 140

Ser Gly Asp Glu Asn Ser Val Leu Thr Thr Ile Ile Lys Asp Asp Ile
145 150 155 160

Leu Ser Ala Val Glu Asn Asn Gln Ser Tyr Thr Asn Ser Asp Lys Ser
165 170 175

His Ser Val Asn Gln Asn Ile Thr Ile Lys Thr Thr Leu Leu Lys Lys

180 185 190

Leu Met Cys Ser Met Gln His Pro Pro Ser Trp Leu Ile His Trp Phe
195 200 205

Asn Leu Tyr Thr Lys Leu Asn Asn Ile Leu Thr Gln Tyr Arg Ser Asn
210 215 220

Glu Val Lys Ser His Gly Phe Ile Leu Ile Asp Asn Gln Thr Leu Ser
225 230 235 240

Gly Phe Gln Phe Ile Leu Asn Gln Tyr Gly Cys Ile Val Tyr His Lys
245 250 255

Gly Leu Lys Lys Ile Thr Thr Thr Thr Tyr Asn Gln Phe Leu Thr Trp
260 265 270

Lys Asp Ile Ser Leu Ser Arg Leu Asn Val Cys Leu Ile Thr Trp Ile
275 280 285

Ser Asn Cys Leu Asn Thr Leu Asn Lys Ser Leu Gly Leu Arg Cys Gly
290 295 300

Phe Asn Asn Val Val Leu Ser Gln Leu Phe Leu Tyr Gly Asp Cys Ile
305 310 315 320

Leu Lys Leu Phe His Asn Glu Gly Phe Tyr Ile Ile Lys Glu Val Glu
325 330 335

Gly Phe Ile Met Ser Leu Ile Leu Asn Ile Thr Glu Glu Asp Gln Phe
340 345 350

Arg Lys Arg Phe Tyr Asn Ser Met Leu Asn Asn Ile Thr Asp Ala Ala
355 360 365

Ile Lys Ala Gln Lys Asp Leu Leu Ser Arg Val Cys His Thr Leu Leu
370 375 380

Asp Lys Thr Val Ser Asp Asn Ile Ile Asn Gly Lys Trp Ile Ile Leu
385 390 395 400

Leu Ser Lys Phe Leu Lys Leu Ile Lys Leu Ala Gly Asp Asn Asn Leu
405 410 415

Asn Asn Leu Ser Glu Leu Tyr Phe Leu Phe Arg Ile Phe Gly His Pro
420 425 430

Met Val Asp Glu Arg Gln Ala Met Asp Ser Val Arg Ile Asn Cys Asn
435 440 445

Glu Thr Lys Phe Tyr Leu Leu Ser Ser Leu Ser Thr Leu Arg Gly Ala
450 455 460

Phe Ile Tyr Arg Ile Ile Lys Gly Phe Val Asn Thr Tyr Asn Arg Trp
465 470 475 480

Pro Thr Leu Arg Asn Ala Ile Val Leu Pro Leu Arg Trp Leu Asn Tyr
485 490 495

Tyr Lys Leu Asn Thr Tyr Pro Ser Leu Leu Glu Ile Thr Glu Asn Asp
500 505 510

Leu Ile Ile Leu Ser Gly Leu Arg Phe Tyr Arg Glu Phe His Leu Pro
515 520 525

Lys Lys Val Asp Leu Glu Met Ile Ile Asn Asp Lys Ala Ile Ser Pro
530 535 540

Pro Lys Asp Leu Ile Trp Thr Ser Phe Pro Arg Asn Tyr Met Pro Ser
545 550 555 560

His Ile Gln Asn Tyr Ile Glu His Glu Lys Leu Lys Phe Ser Glu Ser
565 570 575

Asp Arg Ser Arg Arg Val Leu Glu Tyr Tyr Leu Arg Asp Asn Lys Phe
580 585 590

Asn Glu Cys Asp Leu Tyr Asn Cys Val Val Asn Gln Ser Tyr Leu Asn
595 600 605

Asn Ser Asn His Val Val Ser Leu Thr Gly Lys Glu Arg Glu Leu Ser
610 615 620

Val Gly Arg Met Phe Ala Met Gln Pro Gly Met Phe Arg Gln Ile Gln
625 630 635 640

Ile Leu Ala Glu Lys Met Ile Ala Glu Asn Ile Leu Gln Phe Phe Pro
645 650 655

Glu Ser Leu Thr Arg Tyr Gly Asp Leu Glu Leu Gln Lys Ile Leu Glu
660 665 670

Leu Lys Ala Gly Ile Ser Asn Lys Ser Asn Arg Tyr Asn Asp Asn Tyr
675 680 685

Asn Asn Tyr Ile Ser Lys Cys Ser Ile Ile Thr Asp Leu Ser Lys Phe
690 695 700

Asn Gln Ala Phe Arg Tyr Glu Thr Ser Cys Ile Cys Ser Asp Val Leu
705 710 715 720

Asp Glu Leu His Gly Val Gln Ser Leu Phe Ser Trp Leu His Leu Thr
725 730 735

Ile Pro Leu Val Thr Ile Ile Cys Thr Tyr Arg His Ala Pro Pro Phe
740 745 750

Ile Lys Asp His Val Val Asn Leu Asn Glu Val Asp Glu Gln Ser Gly
755 760 765

Leu Tyr Arg Tyr His Met Gly Gly Ile Glu Gly Trp Cys Gln Lys Leu
770 775 780

Trp Thr Ile Glu Ala Ile Ser Leu Leu Asp Leu Ile Ser Leu Lys Gly
785 790 795 800

Lys Phe Ser Ile Thr Ala Leu Ile Asn Gly Asp Asn Gln Ser Ile Asp
805 810 815

Ile Ser Lys Pro Val Arg Leu Ile Glu Gly Gln Thr His Ala Gln Ala
820 825 830

Asp Tyr Leu Leu Ala Leu Asn Ser Leu Lys Leu Leu Tyr Lys Glu Tyr
835 840 845

Ala Gly Ile Gly His Lys Leu Lys Gly Thr Glu Thr Tyr Ile Ser Arg
850 855 860

Asp Met Gln Phe Met Ser Lys Thr Ile Gln His Asn Gly Val Tyr Tyr
865 870 875 880

Pro Ala Ser Ile Lys Lys Val Leu Arg Val Gly Pro Trp Ile Asn Thr
885 890 895

Ile Leu Asp Asp Phe Lys Val Ser Leu Glu Ser Ile Gly Ser Leu Thr
900 905 910

Gln Glu Leu Glu Tyr Arg Gly Glu Ser Leu Leu Cys Ser Leu Ile Phe
915 920 925

Arg Asn Ile Trp Leu Tyr Asn Gln Ile Ala Leu Gln Leu Arg Asn His
930 935 940

Ala Leu Cys Asn Asn Lys Leu Tyr Leu Asp Ile Leu Lys Val Leu Lys
945 950 955 960

His Leu Lys Thr Phe Phe Asn Leu Asp Ser Ile Asp Met Ala Leu Ser
965 970 975

Leu Tyr Met Asn Leu Pro Met Leu Phe Gly Gly Gly Asp Pro Asn Leu
980 985 990

Leu Tyr Arg Ser Phe Tyr Arg Arg Thr Pro Asp Phe Leu Thr Glu Ala
995 1000 1005

Ile Val His Ser Val Phe Val Leu Ser Tyr Tyr Thr Gly His Asp Leu

1010 1015 1020

Gln Asp Lys Leu Gln Asp Leu Pro Asp Asp Arg Leu Asn Lys Phe Leu
1025 1030 1035 1040

Thr Cys Val Ile Thr Phe Asp Lys Asn Pro Asn Ala Glu Phe Val Thr
1045 1050 1055

Leu Met Arg Asp Pro Gln Ala Leu Gly Ser Glu Arg Gln Ala Lys Ile
1060 1065 1070

Thr Ser Glu Ile Asn Arg Leu Ala Val Thr Glu Val Leu Ser Ile Ala
1075 1080 1085

Pro Asn Lys Ile Phe Ser Lys Ser Ala Gln His Tyr Thr Thr Thr Glu
1090 1095 1100

Ile Asp Leu Asn Asp Ile Met Gln Asn Ile Glu Pro Thr Tyr Pro His
1105 1110 1115 1120

Gly Leu Arg Val Val Tyr Glu Ser Leu Pro Phe Tyr Lys Ala Glu Lys
1125 1130 1135

Ile Val Asn Leu Ile Ser Gly Thr Lys Ser Ile Thr Asn Ile Leu Glu
1140 1145 1150

Lys Thr Ser Ala Ile Asp Thr Thr Asp Ile Asn Arg Ala Thr Asp Met
1155 1160 1165

Met Arg Lys Asn Ile Thr Leu Leu Ile Arg Ile Leu Pro Leu Asp Cys
1170 1175 1180

Asn Lys Asp Lys Arg Glu Leu Leu Ser Leu Glu Asn Leu Ser Ile Thr
1185 1190 1195 1200

Glu Leu Ser Lys Tyr Val Arg Glu Arg Ser Trp Ser Leu Ser Asn Ile
1205 1210 1215

Val Gly Val Thr Ser Pro Ser Ile Met Phe Thr Met Asp Ile Lys Tyr
1220 1225 1230

Thr Thr Ser Thr Ile Ala Ser Gly Ile Ile Ile Glu Lys Tyr Asn Val
1235 1240 1245

Asn Ser Leu Thr Arg Gly Glu Arg Gly Pro Thr Lys Pro Trp Val Gly
1250 1255 1260

Ser Ser Thr Gln Glu Lys Lys Thr Met Pro Val Tyr Asn Arg Gln Val
1265 1270 1275 1280

Leu Thr Lys Lys Gln Arg Asp Gln Ile Asp Leu Leu Ala Lys Leu Asp
1285 1290 1295

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Trp Val Tyr Ala Ser Ile Asp Asn Lys Asp Glu Phe Met Glu Glu Leu
            1300                1305                1310

Ser Thr Gly Thr Leu Gly Leu Ser Tyr Glu Lys Ala Lys Lys Leu Phe
        1315                1320                1325

Pro Gln Tyr Leu Ser Val Asn Tyr Leu His Arg Leu Thr Val Ser Ser
    1330                1335                1340

Arg Pro Cys Glu Phe Pro Ala Ser Ile Pro Ala Tyr Arg Thr Thr Asn
1345                1350                1355                1360

Tyr His Phe Asp Thr Ser Pro Ile Asn His Val Leu Thr Glu Lys Tyr
                1365                1370                1375

Gly Asp Glu Asp Ile Asp Ile Val Phe Gln Asn Cys Ile Ser Phe Gly
            1380                1385                1390

Leu Ser Leu Met Ser Val Val Glu Gln Phe Thr Asn Ile Cys Pro Asn
        1395                1400                1405

Arg Ile Ile Leu Ile Pro Lys Leu Asn Glu Ile His Leu Met Lys Pro
    1410                1415                1420

Pro Ile Phe Thr Gly Asp Val Asp Ile Ile Lys Leu Lys Gln Val Ile
1425                1430                1435                1440

Gln Lys Gln His Met Phe Leu Pro Asp Lys Ile Ser Leu Thr Gln Tyr
                1445                1450                1455

Val Glu Leu Phe Leu Ser Asn Lys Ala Leu Lys Ser Gly Ser His Ile
            1460                1465                1470

Asn Ser Asn Leu Ile Leu Val His Lys Met Ser Asp Tyr Phe His Asn
        1475                1480                1485

Ala Tyr Ile Leu Ser Thr Asn Leu Ala Gly His Trp Ile Leu Ile Ile
    1490                1495                1500

Gln Leu Met Lys Asp Ser Lys Gly Ile Phe Glu Lys Asp Trp Gly Glu
1505                1510                1515                1520

Gly Tyr Ile Thr Asp His Met Phe Ile Asn Leu Asn Val Phe Phe Asn
                1525                1530                1535

Ala Tyr Lys Thr Tyr Leu Leu Cys Phe His Lys Gly Tyr Gly Lys Ala
            1540                1545                1550

Lys Leu Glu Cys Asp Met Asn Thr Ser Asp Leu Leu Cys Val Leu Glu
        1555                1560                1565
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Leu Ile Asp Ser Ser Tyr Trp Lys Ser Met Ser Lys Val Phe Leu Glu
1570 1575 1580

Gln Lys Val Ile Lys Tyr Ile Val Asn Gln Asp Thr Ser Leu Arg Arg
1585 1590 1595 1600

Ile Lys Gly Cys His Ser Phe Lys Leu Trp Phe Leu Lys Arg Leu Asn
1605 1610 1615

Asn Ala Lys Phe Thr Val Cys Pro Trp Val Val Asn Ile Asp Tyr His
1620 1625 1630

Pro Thr His Met Lys Ala Ile Leu Ser Tyr Ile Asp Leu Val Arg Met
1635 1640 1645

Gly Leu Ile Asn Val Asp Lys Leu Thr Ile Lys Asn Lys Asn Lys Phe
1650 1655 1660

Asn Asp Glu Phe Tyr Thr Ser Asn Leu Phe Tyr Ile Ser Tyr Asn Phe
1665 1670 1675 1680

Ser Asp Asn Thr His Leu Leu Thr Lys Gln Ile Arg Ile Ala Asn Ser
1685 1690 1695

Glu Leu Glu Asp Asn Tyr Asn Lys Leu Tyr His Pro Thr Pro Glu Thr
1700 1705 1710

Leu Glu Asn Met Ser Leu Ile Pro Val Lys Ser Asn Asn Ser Asn Lys
1715 1720 1725

Pro Lys Phe Cys Ile Ser Gly Asn Thr Glu Ser Met Met Met Ser Thr
1730 1735 1740

Phe Ser Ser Lys Met His Ile Lys Ser Ser Thr Val Thr Thr Arg Phe
1745 1750 1755 1760

Asn Tyr Ser Lys Gln Asp Leu Tyr Asn Leu Phe Pro Ile Val Val Ile
1765 1770 1775

Asp Lys Ile Ile Asp His Ser Gly Asn Thr Ala Lys Ser Asn Gln Leu
1780 1785 1790

Tyr Thr Thr Thr Ser His Gln Thr Ser Leu Val Arg Asn Ser Ala Ser
1795 1800 1805

Leu Tyr Cys Met Leu Pro Trp His His Val Asn Arg Phe Asn Phe Val
1810 1815 1820

Phe Ser Ser Thr Gly Cys Lys Ile Ser Ile Glu Tyr Ile Leu Lys Asp
1825 1830 1835 1840

Leu Lys Ile Lys Asp Pro Ser Cys Ile Ala Phe Ile Gly Glu Gly Ala

1845 1850 1855

Gly Asn Leu Leu Leu Arg Thr Val Val Glu Leu His Pro Asp Ile Arg
1860 1865 1870

Tyr Ile Tyr Arg Ser Leu Lys Asp Cys Asn Asp His Ser Leu Pro Ile
1875 1880 1885

Glu Phe Leu Arg Leu Tyr Asn Gly His Ile Asn Ile Asp Tyr Gly Glu
1890 1895 1900

Asn Leu Thr Ile Pro Ala Thr Asp Ala Thr Asn Asn Ile His Trp Ser
1905 1910 1915 1920

Tyr Leu His Ile Lys Phe Ala Glu Pro Ile Ser Ile Phe Val Cys Asp
1925 1930 1935

Ala Glu Leu Pro Val Thr Ala Asn Trp Ser Lys Ile Ile Ile Glu Trp
1940 1945 1950

Ser Lys His Val Arg Lys Cys Lys Tyr Cys Ser Ser Val Asn Arg Cys
1955 1960 1965

Ile Leu Ile Ala Lys Tyr His Ala Gln Asp Asp Ile Asp Phe Lys Leu
1970 1975 1980

Asp Asn Ile Thr Ile Leu Lys Thr Tyr Val Cys Leu Gly Ser Lys Leu
1985 1990 1995 2000

Lys Gly Ser Glu Val Tyr Leu Ile Leu Thr Ile Gly Pro Ala Asn Ile
2005 2010 2015

Leu Pro Val Phe Asp Val Val Gln Asn Ala Lys Leu Thr Leu Ser Arg
2020 2025 2030

Thr Lys Asn Phe Ile Met Pro Lys Lys Thr Asp Lys Glu Ser Ile Asp
2035 2040 2045

Ala Asn Ile Lys Ser Leu Ile Pro Phe Leu Cys Tyr Pro Ile Thr Lys
2050 2055 2060

Lys Gly Ile Lys Thr Ser Leu Ser Lys Leu Lys Ser Val Val Asn Gly
2065 2070 2075 2080

Asp Ile Leu Ser Tyr Ser Ile Ala Gly Arg Asn Glu Val Phe Ser Asn
2085 2090 2095

Lys Leu Ile Asn His Lys His Met Asn Ile Leu Lys Trp Leu Asp His
2100 2105 2110

Val Leu Asn Phe Arg Ser Ala Glu Leu Asn Tyr Asn His Leu Tyr Met
2115 2120 2125

Ile Glu Ser Thr Tyr Pro Tyr Leu Ser Glu Leu Leu Asn Ser Leu Thr
    2130   2135   2140

Thr Asn Glu Leu Lys Lys Leu Ile Lys Ile Thr Gly Ser Val Leu Tyr
2145   2150   2155   2160

Asn Leu Pro Asn Glu Gln
                2165

(2) INFORMATION FOR SEQ ID NO:25:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 15229 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:

ACGCGAAAAA ATGCGTACTA CAAACTTGCA CATTCGGAAA AAATGGGGCA AATAAGAATT 60

TGATAAGTGC TATTTAAATC TAACCTTTTC AATCAGAAAT GGGGTGCAAT TCACTGAGCA 120

TGATAAAGGT TAGATTACAA AATTTATTTG ACAATGACGA AGTAGCATTG TTAAAAATAA 180

CATGTTATAC TGACAAATTA ATTCTTCTGA CCAATGCATT AGCCAAAGCA GTAATACATA 240

CAATTAAATT AAACGGCATA GTTTTTATAC ATGTTATAAC AAGCAGTGAA GTGTGCCCTG 300

ACAACAATAT TGTAGTGAAA TCTAACTTTA CAACAATGCC AATATTACAA AACGGAGGAT 360

ACATATGGGA ATTGATTGAG TTGACACACT GCTCTCAATC AAATGGTCTA ATGGATGATA 420

ATTGTGAAAT CAAATTTTCT AAAAGACTAA GTGACTCAGT AATGACTAAT TATATGAATC 480

AAATATCTGA TTTACTTGGG CTTGATCTCA ATTCATGAAT TATGTTTAGT CTAATTTAAT 540

AGACATGTGT TTATCACCAT TTTAGTTAAT ATAAAACCTC ATCAAAGGGA AATGGGGCAA 600

ATAAACTCAC CTAATCAGTC AAACCATGAG CACTACAAAT GACAACACTA CTATGCAAAG 660

ATTGATGATC ACAGACATGA GACCCCTGTC GATGGAATCA ATAATAACAT CTCTCACCAA 720

AGAAATCATA ACACACAAAT TCATATACTT GATAAACAAT GAATGTATTG TAAGAAAACT 780

TGATGAAAGA CAAGCTACAT TTACATTCTT AGTCAATTAT GAGATGAAGC TATTGCACAA 840

AGTAGGGAGT ACCAAATACA AGAAATACAC TGAATATAAT ACAAAATATG GCACTTTCCC 900
CATGCCTATA TTTATCAATC ATGACGGGTT TCTAGAATGT ATTGGCATTA AGCCTACAAA 960
ACACACTCCT ATAATATACA AATATGACCT CAACCCGTAA ATTCCAACAA AAAACTAACC 1020
CATCCAAACT AAGCTATTCC TCAAACAACA GTGCTCAACA GTTAAGAAGG AGCTAATCCA 1080
TTTTAGTAAT TAAAAATAAA GGCAGAGCCA ATAACATAAA TTGGGGCAAA TACAAAGATG 1140
GCTCTTAGCA AAGTCAAGTT AAATGATACA TTAAATAAGG ATCAGCTGCT GTCATCCAGC 1200
AAATACACTA TTCAACGTAG TACAGGAGAT AATATTGACA CTCCCAATTA TGATGTGCAA 1260
AAACACCTAA ACAAACTATG TGGTATGCTA TTAATCACTG AAGATGCAAA TCATAAATTC 1320
ACAGGATTAA TAGGTATGTT ATATGCTATG TCCAGGTTAG GAAGGGAAGA CACTATAAAG 1380
ATACTTAAAG ATGCTGGATA TCATGTTAAA GCTAATGGAG TAGATATAAC AACATATCGT 1440
CAAGATATAA ACGGAAAGGA AATGAAATTC GAAGTATTAA CATTATCAAG CTTGACATCA 1500
GAAATACAAG TCAATATTGA GATAGAATCT AGAAAGTCCT ACAAAAAAAT GCTAAAAGAG 1560
ATGGGAGAAG TGGCTCCAGA ATATAGGCAT GATTCTCCAG ACTGTGGGAT GATAATACTG 1620
TGTATAGCTG CACTTGTAAT AACCAAGTTA GCAGCAGGAG ATAGATCAGG TCTTACAGCA 1680
GTAATTAGGA GGGCAAACAA TGTCTTAAAA AACGAAATAA AACGCTACAA GGGCCTCATA 1740
CCAAAGGATA TAGCTAACAG TTTTTATGAA GTGTTTGAAA AACACCCTCA TCTTATAGAT 1800
GTTTTTGTGC ACTTTGGCAT TGCACAATCA TCCACAAGAG GGGGTAGTAG AGTTGAAGGA 1860
ATCTTTGCAG GATTATTTAT GAATGCCTAT GGTTCAGGGC AAGTAATGCT AAGATGGGGA 1920
GTTCTAGCCA AATCTGTAAA AAATATCATG CTAGGACATG CTAGTGTCCA GGCAGAAATG 1980
GAACAAGTTG TGGAAGTTTA TGAGTATGCA CAGAAGTTGG GAGGAGAAGC TGGATTCTAC 2040
CATATATTGA ACAATCCAAA AGCATCATTG CTGTCATTAA CTCAATTTCC TAACTTCTCA 2100
AGTGTGGTCC TAGGCAATGC AGCAGGTCTA GGCATAATGG GAGAGTATAG AGGTACACCA 2160
AGAAACCAAG ATCTATATGA TGCAGCCAAA GCATATGCAG AGCAACTCAA AGAAAATGGA 2220
GTAATAAACT ACAGTGTATT AGACTTAACA GCAGAAGAAT TGGAAGCCAT AAAGCATCAA 2280
CTCAACCCCA AAGAAGATGA TGTAGAGCTT TAAGTTAACA AAAAATACGG GGCAAATAAG 2340
TCAACATGGA GAAGTTTGCA CCTGAATTTC ATGGAGAAGA TGCAAACAAC AAAGCTACCA 2400

AATTCCTAGA ATCAATAAAG GGCAAGTTTG CATCATCCAA AGATCCTAAG AAGAAAGATA 2460

GCATAATATC TGTTAACTCA ATAGATATAG AAGTAACTAA AGAGAGCCCG ATAACATCTG 2520

GCACCAACAT CATCAATCCA ATAAGTGAAG CTGATAGTAC CCCAGAAGCT AAAGCCAACT 2580

ACCCAAGAAA ACCCCTAGTA AGCTTCAAAG AAGATCTCAC CCCAAGTGAC AACCCCTTTT 2640

CTAAGTTGTA CAAAGAAACA ATAGAAACAT TTGATAACAA TGAAGAAGAA TCTAGCTACT 2700

CATATGAAGA AATAAATGAT CAAACAAATG ACAACATTAC AGCAAGACTA GATAGAATTG 2760

ATGAAAAATT AAGTGAAATA TTAGGAATGC TCCATACATT AGTAGTTGCA AGTGCAGGAC 2820

CCACCTCAGC TCGCGATGGA ATAAGAGATG CTATGGTTGG TCTAAGAGAA GAAATGATAG 2880

AAAAAATAAG AGCGGAAGCA TTAATGACCA ATGATAGGTT AGAGGCTATG GCAAGACTTA 2940

GGAATGAGGA AAGCGAAAAA ATGGCAAAAG ACACCTCAGA TGAAGTGTCT CTTAATCCAA 3000

CTTCCAAAAA ATTGAGTAAT TTGTTGGAAG ACAACGATAG TGACAATGAT CTATCACTTG 3060

ATGATTTTTG ATCAGTGATC AACTCACTCA GCAATCAACA ACATCAATGA AACAGACATC 3120

AATCCATTGA ATCAACTGCC AGACTGAACA CACAAACGTC CATCAGCAGA ACTACCAACC 3180

AATCAATCAA CCAATTGATC AATCAGCGAC CTAACAAAAT TAACAATATA GTAACAAAAA 3240

AAGAACAAGA TGGGGCAAAT ATGGAAACAT ACGTGAACAA GCTTCACGAG GGCTCCACAT 3300

ACACAGCAGC TGTTCAGTAC AATGTTCTAG AAAAAGATGA TGATCCTGCA TCACTAACAA 3360

TATGGGTGCC TATGTTCCAG TCATCTGTGC CAGCAGACTT GCTCATAAAA GAACTTGCAA 3420

GCATCAACAT ACTAGTGAAG CAGATCTCCA CGCCCAAAGG ACCTTCACTA CGAGTCACGA 3480

TTAACTCAAG AAGTGCTGTG CTGGCACAAA TGCCTAGTAG TTTTATCATA AGTGCAAATG 3540

TATCATTAGA TGAAAGAAGC AAATTAGCAT ATGATGTAAC TACACCTTGT GAAATCAAAG 3600

CATGCAGTCT AACATGCTTA AAAGTAAAAA GTATGTTAAC TACAGTCAAA GATCTTACCA 3660

TGAAAACATT CAATCCCACT CATGAGATTA TTGCTCTATG TGAATTTGAA AATATTATGA 3720

CATCAAAAAG AGTAATAATA CCAACCTATC TAAGATCAAT TAGTGTCAAA AACAAGGACC 3780

TGAACTCACT AGAAAATATA GCAACCACCG AATTCAAAAA TGCTATCACC AATGCGAAAA 3840

TTATTCCCTA TGCAGGATTA GTATTAGTTA TCACAGTTAC TGACAATAAA GGAGCATTCA 3900

AATATATCAA GCCACAGAGT CAATTTATAG TAGATCTTGG GGCCTACCTA GAAAAAGAGA 3960

GCATATATTA TGTGACTACA AATTGGAAGC ATACAGCTAC ACGTTTTTCA ATCAAACCAC 4020

TAGAGGATTA AACTTAATTA TCAACACTAA ATGACAGGTC CACATATATC TTCAAACTAT 4080

ACATTATATC CAAACATCAT GAGCATTTAC ACTACACACT TTTACCATAT AAATCAATCT 4140

CATTTAAAAT CCAAAATTAC TTCCAGCTAT CATCTGTTAG ACCTAGAGTG CGAATAGGTA 4200

AATAAAACCA AAATATGGGG TAAATAGACA TTAGTTAGAG TTCAATCAAT CTCAACAACC 4260

ATTTATACCG CCAATTCAGT ACATATACTA TAAATCTCAA AATGGGAAAT ACATCCATCA 4320

CAATAGAATT CACAAGCAAA TTTTGGCCTT ATTTTACACT AATACATATG ATCTTAACTC 4380

TAATCTCTTT ACTAATTATA ATCACTATTA TGATTGCAAT ACTAAATAAG CTAAGTGAAC 4440

ATAAAACATT CTGCAACAAA ACTCTTGAAC TAGGACAGAT GTATCAAATC AACACATAGT 4500

GTTCTACCAT TATGCTGTGT CAAATTATAA TCTTGTATAT ATAAACAAAC AAATCCAATC 4560

TTCTCACAGA GTCATGGTGG CGCAAAACCA CGCCAACCAT CATGATAGCA TAGAGTAGTT 4620

ATTTAAAAAT TAACATAATG ATGAATTATT GGTATGAGAT CAGGAACAAC ATTGGGGCAA 4680

ATGCAGCCAT GTCCAAGCAC AAGAATCGGC GCACTGCCGG GACTCTAGAA AGGACCTGGG 4740

ATACTCTTAA TCATCTAATT GTAATATCCT CTTGTTTATA CAGATTAAAT TTAAAATCTA 4800

TAGCACAAAT AGCACTGTCA GTTTTGGCAA TGATAATCTC AACCTCTCTC ATAATTGCAG 4860

CCATAATATT CATCATCTCT GCCAATCACA AAGTTACACT AACAACGGTT ACAGTTCAAA 4920

CAATAAAAAA CCACACTGAA AAAAACATCT CCACCTACCT TACTCAAGTC CCACCAGAAA 4980

GGGTCAACTC ATCCAAACAA CCCACAACCA CATCACCAAT CCACACAAAT TCAGCCACAA 5040

TATCACCAAA TACAAAATCA GAAACACACC ATACAACAGC ACAAACCAAA GGCAGAATCA 5100

CCACTTCAAC ACAGACCAAC AAGCCAAGCA CAAAATCACG TTCAAAAAAT CCACCAAAAA 5160

AACCAAAAGA TGATTACCAT TTTGAAGTGT TCAATTTTGT TCCCTGTAGT ATATGTGGTA 5220

ATAATCAACT CTGCAAATCC ATCTGCAAAA CAATACCAAG CAACAAACCA AAGAAAAAAC 5280

CAACCATCAA ACCCACAAAC AAACCAACCA CCAAAACCAC AAACAAAAGA GACCCCAAAA 5340

CACCAGCCAA AATGCCAAAA AAAGAAATCA TCACCAACCC AGCAAAAAAA CCAACCCTCA 5400

AGACCACAGA AAGAGACACC AGCATTTCAC AATCCACCGT GCTCGACACA ATCACTCCAA 5460

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CACAAATACC CACAGCATCC GAGCCCTCCA CATTAAATCC TAATTAAAAA ACCTAGTCAC 5580

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AAAGTTATCA TTTTGGTCTT AAGGGGTTGA ATAAAAATCT AAAACTAACA ATTATACATG 15180

TGCATTTACA ACACAACGAG ACATTAGTTT TTGACACTTT TTTTCTCGT 15229

(2) INFORMATION FOR SEQ ID NO:26:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2166 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:

Met Asp Pro Ile Ile Asn Gly Asn Ser Ala Asn Val Tyr Leu Thr Asp
1 5 10 15

Ser Tyr Leu Lys Gly Val Ile Ser Phe Ser Glu Cys Asn Ala Leu Gly
20 25 30

Ser Tyr Leu Phe Asn Gly Pro Tyr Leu Lys Asn Asp Tyr Thr Asn Leu
35 40 45

Ile Ser Arg Gln Ser Pro Leu Leu Glu His Met Asn Leu Lys Lys Leu
50 55 60

Thr Ile Thr Gln Ser Leu Ile Ser Arg Tyr His Lys Gly Glu Leu Lys
65 70 75 80

Leu Glu Glu Pro Thr Tyr Phe Gln Ser Leu Leu Met Thr Tyr Lys Ser
85 90 95

Met Ser Ser Ser Glu Gln Ile Ala Thr Thr Asn Leu Leu Lys Lys Ile
100 105 110

Ile Arg Arg Ala Ile Glu Ile Ser Asp Val Lys Val Tyr Ala Ile Leu
115 120 125

Asn Lys Leu Gly Leu Lys Glu Lys Asp Arg Val Lys Pro Asn Asn Asn
130 135 140

Ser Gly Asp Glu Asn Ser Val Leu Thr Thr Ile Ile Lys Asp Asp Ile
145 150 155 160

Leu Ser Ala Val Glu Asn Asn Gln Ser Tyr Thr Asn Ser Asp Lys Asn
165 170 175

His Ser Val Asn Gln Asn Ile Thr Ile Lys Thr Thr Leu Leu Lys Lys
180 185 190

Leu Met Cys Ser Met Gln His Pro Pro Ser Trp Leu Ile His Trp Phe
195 200 205

Asn Leu Tyr Thr Lys Leu Asn Asn Ile Leu Thr Gln Tyr Arg Ser Asn
210 215 220

Glu Val Lys Ser His Gly Phe Ile Leu Ile Asp Asn Gln Thr Leu Ser
225 230 235 240

Asp Phe Gln Phe Ile Leu Asn Gln Tyr Gly Cys Ile Val Tyr His Lys
245 250 255

Gly Leu Lys Lys Ile Thr Thr Thr Thr Tyr Asn Gln Phe Leu Thr Trp
260 265 270

Lys Asp Ile Ser Leu Ser Arg Leu Asn Val Cys Leu Ile Thr Trp Ile
275 280 285

Ser Asn Cys Leu Asn Thr Leu Asn Lys Ser Leu Gly Leu Arg Cys Gly
290 295 300

Phe Asn Asn Val Val Leu Ser Gln Leu Phe Leu Tyr Gly Asp Cys Ile
305 310 315 320

Leu Lys Leu Phe His Asn Glu Gly Phe Tyr Ile Ile Lys Glu Val Glu
325 330 335

Gly Phe Ile Met Ser Leu Ile Leu Asn Ile Thr Glu Glu Asp Gln Phe
340 345 350

Arg Lys Arg Phe Tyr Asn Ser Met Leu Asn Asn Ile Thr Asp Ala Ala
355 360 365

Ile Lys Ala Gln Lys Asn Leu Leu Ser Arg Val Cys His Thr Leu Leu
370 375 380

Asp Lys Thr Val Ser Asp Asn Ile Ile Asn Gly Lys Trp Ile Ile Leu
385 390 395 400

Leu Ser Lys Phe Leu Lys Leu Ile Lys Leu Ala Gly Asp Asn Asn Leu

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                    405                 410                 415

Asn Asn Leu Ser Glu Leu Tyr Phe Leu Phe Arg Ile Phe Gly His Pro
                420                 425                 430

Met Val Asp Glu Arg Gln Ala Met Asp Ala Val Arg Ile Asn Cys Asn
            435                 440                 445

Glu Thr Lys Phe Tyr Leu Leu Ser Asn Leu Ser Thr Leu Arg Gly Ala
    450                 455                 460

Phe Ile Tyr Arg Ile Ile Lys Gly Phe Val Asn Thr Tyr Asn Arg Trp
465                 470                 475                 480

Pro Thr Leu Arg Asn Ala Ile Val Leu Pro Leu Arg Trp Leu Asn Tyr
                    485                 490                 495

Tyr Lys Leu Asn Thr Tyr Pro Ser Leu Leu Glu Ile Thr Glu Lys Asp
                500                 505                 510

Leu Ile Ile Leu Ser Gly Leu Arg Phe Tyr Arg Glu Phe His Leu Pro
            515                 520                 525

Lys Lys Val Asp Leu Glu Met Ile Ile Asn Asp Lys Ala Ile Ser Pro
    530                 535                 540

Pro Lys Asp Leu Ile Trp Thr Ser Phe Pro Arg Asn Tyr Met Pro Ser
545                 550                 555                 560

His Ile Gln Asn Tyr Ile Glu His Glu Lys Leu Lys Phe Ser Glu Ser
                    565                 570                 575

Asp Arg Ser Arg Arg Val Leu Glu Tyr Tyr Leu Arg Asp Asn Lys Phe
                580                 585                 590

Asn Glu Cys Asp Leu Tyr Asn Cys Val Val Asn Gln Ser Tyr Leu Asn
            595                 600                 605

Asn Ser Asn His Val Val Ser Leu Thr Gly Lys Glu Arg Glu Leu Ser
    610                 615                 620

Val Gly Arg Met Phe Ala Met Gln Pro Gly Met Phe Arg Gln Ile Gln
625                 630                 635                 640

Ile Leu Ala Glu Lys Met Ile Ala Glu Asn Ile Leu Gln Phe Phe Pro
                    645                 650                 655

Glu Ser Leu Thr Arg Tyr Gly Asp Leu Glu Leu Gln Lys Ile Leu Glu
                660                 665                 670

Leu Lys Ala Gly Ile Ser Asn Lys Ser Asn Arg Tyr Asn Asp Asn Tyr
            675                 680                 685
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Asn Asn Tyr Ile Ser Lys Cys Ser Ile Ile Thr Asp Leu Ser Lys Phe
    690                 695                 700

Asn Gln Ala Phe Arg Tyr Glu Thr Ser Cys Ile Cys Ser Asp Val Leu
705                 710                 715                 720

Asp Glu Leu His Gly Val Gln Ser Leu Phe Ser Trp Leu His Leu Thr
                725                 730                 735

Ile Pro Leu Val Thr Ile Ile Cys Thr Tyr Arg His Ala Pro Pro Phe
            740                 745                 750

Ile Lys Asp His Val Val Asn Leu Asn Lys Val Asp Glu Gln Ser Gly
        755                 760                 765

Leu Tyr Arg Tyr His Met Gly Gly Ile Glu Gly Trp Cys Gln Lys Leu
    770                 775                 780

Trp Thr Ile Glu Ala Ile Ser Leu Leu Asp Leu Ile Ser Leu Lys Gly
785                 790                 795                 800

Lys Phe Ser Ile Thr Ala Leu Ile Asn Gly Asp Asn Gln Ser Ile Asp
                805                 810                 815

Ile Ser Lys Pro Val Arg Leu Ile Glu Gly Gln Thr His Ala Gln Ala
            820                 825                 830

Asp Tyr Leu Leu Ala Leu Asn Ser Leu Lys Leu Leu Tyr Lys Glu Tyr
        835                 840                 845

Ala Gly Ile Gly His Lys Leu Lys Gly Thr Glu Thr Tyr Ile Ser Arg
    850                 855                 860

Asp Met Gln Phe Met Ser Lys Thr Ile Gln His Asn Gly Val Tyr Tyr
865                 870                 875                 880

Pro Ala Ser Ile Lys Lys Val Leu Arg Val Gly Pro Trp Ile Asn Thr
                885                 890                 895

Ile Leu Asp Asp Phe Lys Val Ser Leu Glu Ser Ile Gly Ser Leu Thr
            900                 905                 910

Gln Glu Leu Glu Tyr Arg Gly Glu Ser Leu Leu Cys Ser Leu Ile Phe
        915                 920                 925

Arg Asn Ile Trp Leu Tyr Asn Gln Ile Ala Leu Gln Leu Arg Asn His
    930                 935                 940

Ala Leu Cys His Asn Lys Leu Tyr Leu Asp Ile Leu Lys Val Leu Lys
945                 950                 955                 960
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His Leu Lys Thr Phe Phe Asn Leu Asp Ser Ile Asp Met Ala Leu Thr
965 970 975

Leu Tyr Met Asn Leu Pro Met Leu Phe Gly Gly Gly Asp Pro Asn Leu
980 985 990

Leu Tyr Arg Ser Phe Tyr Arg Arg Thr Pro Asp Phe Leu Thr Glu Ala
995 1000 1005

Ile Val His Ser Val Phe Val Leu Ser Tyr Tyr Thr Gly His Asp Leu
1010 1015 1020

Gln Asp Lys Leu Gln Asp Leu Pro Asp Asp Arg Leu Asn Lys Phe Leu
1025 1030 1035 1040

Thr Cys Ile Ile Thr Phe Asp Lys Asn Pro Asn Ala Glu Phe Val Thr
1045 1050 1055

Leu Met Arg Asp Pro Gln Ala Leu Gly Ser Glu Arg Gln Ala Lys Ile
1060 1065 1070

Thr Ser Glu Ile Asn Arg Leu Ala Val Thr Glu Val Leu Ser Ile Ala
1075 1080 1085

Pro Asn Lys Ile Phe Ser Lys Ser Ala Gln His Tyr Thr Thr Thr Glu
1090 1095 1100

Ile Asp Leu Asn Asp Ile Met Gln Asn Ile Glu Pro Thr Tyr Pro His
1105 1110 1115 1120

Gly Leu Arg Val Val Tyr Glu Ser Leu Pro Phe Tyr Lys Ala Glu Lys
1125 1130 1135

Ile Val Asn Leu Ile Ser Gly Thr Lys Ser Ile Thr Asn Ile Leu Glu
1140 1145 1150

Lys Thr Ser Ala Ile Asp Ser Thr Asp Ile Asn Arg Ala Thr Asp Met
1155 1160 1165

Met Arg Lys Asn Ile Thr Leu Leu Ile Arg Ile Leu Pro Leu Asp Cys
1170 1175 1180

Asn Lys Asp Lys Arg Glu Leu Leu Ser Leu Glu Asn Leu Ser Ile Thr
1185 1190 1195 1200

Glu Leu Ser Lys Tyr Val Arg Glu Arg Ser Trp Ser Leu Ser Asn Ile
1205 1210 1215

Val Gly Val Thr Ser Pro Ser Ile Met Phe Thr Met Asp Ile Lys Tyr
1220 1225 1230

Thr Thr Ser Thr Ile Ala Ser Gly Ile Ile Ile Glu Lys Tyr Asn Val

1235 1240 1245

Asn Ser Leu Thr Arg Gly Glu Arg Gly Pro Thr Lys Pro Trp Val Gly
1250 1255 1260

Ser Ser Thr Gln Glu Lys Lys Thr Met Pro Val Tyr Asn Arg Gln Val
1265 1270 1275 1280

Leu Thr Lys Lys Gln Arg Asp Gln Ile Asp Leu Leu Ala Lys Leu Asp
1285 1290 1295

Trp Val Tyr Ala Ser Ile Asp Asn Lys Asp Glu Phe Met Glu Glu Leu
1300 1305 1310

Ser Thr Gly Thr Leu Gly Leu Ser Tyr Glu Lys Ala Lys Lys Leu Phe
1315 1320 1325

Pro Gln Tyr Leu Ser Val Asn Tyr Leu His Arg Leu Thr Val Ser Ser
1330 1335 1340

Arg Pro Cys Glu Phe Pro Ala Ser Ile Pro Ala Tyr Arg Thr Thr Asn
1345 1350 1355 1360

Tyr His Phe Asp Thr Ser Pro Ile Asn His Val Leu Thr Glu Lys Tyr
1365 1370 1375

Gly Asp Glu Asp Ile Asp Ile Val Phe Gln Asn Cys Ile Ser Phe Gly
1380 1385 1390

Leu Ser Leu Met Ser Val Val Glu Gln Phe Thr Asn Ile Cys Pro Asn
1395 1400 1405

Arg Ile Ile Leu Ile Pro Lys Leu Asn Glu Ile His Leu Met Lys Pro
1410 1415 1420

Pro Ile Phe Thr Gly Asp Val Asp Ile Ile Lys Leu Lys Gln Val Ile
1425 1430 1435 1440

Gln Lys Gln His Met Phe Leu Pro Asp Lys Ile Ser Leu Thr Gln Tyr
1445 1450 1455

Val Glu Leu Phe Leu Ser Asn Lys Ala Leu Lys Ser Gly Ser His Ile
1460 1465 1470

Asn Ser Asn Leu Ile Leu Val His Lys Met Ser Asp Tyr Phe His Asn
1475 1480 1485

Ala Tyr Ile Leu Ser Thr Asn Leu Ala Gly His Trp Ile Leu Ile Ile
1490 1495 1500

Gln Leu Met Lys Asp Ser Lys Gly Ile Phe Glu Lys Asp Trp Gly Glu
1505 1510 1515 1520

Gly Tyr Ile Thr Asp His Met Phe Ile Asn Leu Asn Val Phe Phe Asn
1525 1530 1535

Ala Tyr Lys Thr Tyr Leu Leu Cys Phe His Lys Gly Tyr Gly Lys Ala
1540 1545 1550

Lys Leu Glu Cys Asp Met Asn Thr Ser Asp Leu Leu Cys Val Leu Glu
1555 1560 1565

Leu Ile Asp Ser Ser Tyr Trp Lys Ser Met Ser Lys Val Phe Leu Glu
1570 1575 1580

Gln Lys Val Ile Lys Tyr Ile Ile Asn Gln Asp Thr Ser Leu His Arg
1585 1590 1595 1600

Ile Lys Gly Cys His Ser Phe Lys Leu Trp Phe Leu Lys Arg Leu Asn
1605 1610 1615

Asn Ala Lys Phe Thr Val Cys Pro Trp Val Val Asn Ile Asp Tyr His
1620 1625 1630

Pro Thr His Met Lys Ala Ile Leu Ser Tyr Ile Asp Leu Val Arg Met
1635 1640 1645

Gly Leu Ile Asn Val Asp Lys Leu Thr Ile Lys Asn Lys Asn Lys Phe
1650 1655 1660

Asn Asp Glu Phe Tyr Thr Ser Asn Leu Phe Tyr Ile Ser Tyr Asn Phe
1665 1670 1675 1680

Ser Asp Asn Thr His Leu Leu Thr Lys Gln Ile Arg Ile Ala Asn Ser
1685 1690 1695

Glu Leu Glu Asn Asn Tyr Asn Lys Leu Tyr His Pro Thr Pro Glu Thr
1700 1705 1710

Leu Glu Asn Met Ser Leu Ile Pro Val Lys Ser Asn Asn Ser Asn Lys
1715 1720 1725

Pro Lys Phe Gly Ile Ser Gly Asn Thr Glu Ser Met Met Thr Ser Thr
1730 1735 1740

Phe Ser Asn Lys Thr His Ile Lys Ser Ser Ala Val Ile Thr Arg Phe
1745 1750 1755 1760

Asn Tyr Ser Lys Gln Asp Leu Tyr Asn Leu Phe Pro Ile Val Val Ile
1765 1770 1775

Asp Arg Ile Ile Asp His Ser Gly Asn Thr Ala Lys Ser Asn Gln Leu
1780 1785 1790

Tyr Thr Thr Thr Ser His Gln Thr Ser Leu Val Arg Asn Ser Ala Ser
1795 1800 1805

Leu Tyr Cys Met Leu Pro Trp His His Val Asn Arg Phe Asn Phe Val
1810 1815 1820

Phe Ser Ser Thr Gly Cys Lys Ile Ser Ile Glu Tyr Ile Leu Lys Asp
1825 1830 1835 1840

Leu Lys Ile Lys Asp Pro Ser Cys Ile Ala Phe Ile Gly Glu Gly Ala
1845 1850 1855

Gly Asn Leu Leu Leu Arg Thr Val Val Glu Leu His Pro Asp Ile Arg
1860 1865 1870

Tyr Ile Tyr Arg Ser Leu Lys Asp Cys Asn Asp His Ser Leu Pro Ile
1875 1880 1885

Glu Phe Leu Arg Leu Tyr Asn Gly His Ile Asn Ile Asp Tyr Gly Glu
1890 1895 1900

Asn Leu Thr Ile Pro Ala Thr Asp Ala Thr Asn Asn Ile His Trp Ser
1905 1910 1915 1920

Tyr Leu His Ile Lys Phe Ala Glu Pro Ile Ser Ile Phe Val Cys Asp
1925 1930 1935

Ala Glu Leu Pro Val Thr Ala Asn Trp Ser Lys Ile Ile Ile Glu Trp
1940 1945 1950

Ser Lys His Val Arg Lys Cys Lys Tyr Cys Ser Ser Val Asn Arg Cys
1955 1960 1965

Ile Leu Ile Ala Lys Tyr His Ala Gln Asp Asp Ile Asp Phe Lys Leu
1970 1975 1980

Asp Asn Ile Thr Ile Leu Lys Thr Tyr Val Cys Leu Gly Ser Lys Leu
1985 1990 1995 2000

Lys Gly Ser Glu Val Tyr Leu Val Leu Thr Ile Gly Pro Ala Asn Ile
2005 2010 2015

Leu Pro Val Phe Asn Val Val Gln Asn Ala Lys Leu Ile Leu Ser Arg
2020 2025 2030

Thr Lys Asn Phe Ile Met Pro Lys Lys Thr Asp Lys Glu Ser Ile Asp
2035 2040 2045

Ala Asn Ile Lys Ser Leu Ile Pro Phe Leu Cys Tyr Pro Ile Thr Lys
2050 2055 2060

Lys Gly Ile Lys Thr Ser Leu Ser Lys Leu Lys Ser Val Val Ser Gly

2065 2070 2075 2080

Asp Ile Leu Ser Tyr Ser Ile Ala Gly Arg Asn Glu Val Phe Ser Asn
2085 2090 2095

Lys Leu Ile Asn His Lys His Met Asn Ile Leu Lys Trp Leu Asp His
2100 2105 2110

Val Leu Asn Phe Arg Ser Ala Glu Leu Asn Tyr Asn His Leu Tyr Met
2115 2120 2125

Ile Glu Ser Thr Tyr Pro Tyr Leu Ser Glu Leu Leu Asn Ser Leu Thr
2130 2135 2140

Thr Asn Glu Leu Lys Lys Leu Ile Lys Ile Thr Gly Ser Val Leu Tyr
2145 2150 2155 2160

Asn Leu Pro Asn Glu Gln
2165

(2) INFORMATION FOR SEQ ID NO:27:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 15219 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:27:

ACGGGAAAAA AATGCGTACT ACAAACTTGC ACATTCGAAA AAAATGGGGC AAATAAGAAC 60

TTGATAAGTG CTATTTAAGT CTAACCTTTT CAATCAGAAA TGGGGTGCAA TTCACTGAGC 120

ATGATAAAGG TTAGATTACA AAATTTATTT GACAATGACG AAGTAGCATT GTTAAAAATA 180

ACATGTTATA CTGATAAATT AATTCTTCTG ACCAATGCAT TAGCCAAAGC AGCAATACAT 240

ACAATTAAAT TAAACGGCAT AGTTTTTATA CATGTTATAA CAAGCAGTGA AGTGTGCCCT 300

GATAACAATA TTGTAGTGAA ATCTAACTTT ACAACAATGC CAATACTACA AAATGGAGGA 360

TACATATGGG AATTGATTGA GTTGACACAC TGCTCTCAAT TAAACGGTTT AATGGATGAT 420

AATTGTGAAA TCAAATTTTC TAAAAGACTA AGTGACTCAG TAATGACTAA TTATATGAAT 480

CAAATATCTG ACTTACTTGG GCTTGATCTC AATTCATGAA TTATGTTTAG TCTAATTCAA 540

TAGACATGTG TTTATTACCA TTTTAGTTAA TATAAAAACT CATCAAAGGG AAATGGGGCA 600

AATAAACTCA CCTAATCAAT CAAACCATGA GCACTACAAA TGACAACACT ACTATGCAAA 660

GATTGATGAT CACAGACATG AGACCCCTGT CAATGGATTC AATAATAACA TCTCTTACCA 720

AAGAAATCAT CACACACAAA TTCATATACT TGATAAACAA TGAATGTATT GTAAGAAAAC 780

TTGATGAAAG ACAAGCTACA TTTACATTCT TAGTCAATTA TGAGATGAAG CTACTGCACA 840

AAGTAGGGAG TACCAAATAC AAAAAATACA CTGAATATAA TACAAAATAT GGCACTTTCC 900

CCATGCCTAT ATTTATCAAT CACGGCGGGT TTCTAGAATG TATTGGCATT AAGCCTACAA 960

AACACACTCC TATAATATAC AAATATGACC TCAACCCGTG AATTCCAACA AAAAAACCAA 1020

CCCAACCAAA CCAAACTATT CCTCAAACAA CAGTGCTCAA TAGTTAAGAA GGAGCTAATC 1080

CATTTTAGTA ATTAAAAATA AAAGTAAAGC CAATAACATA AATTGGGGCA AATACAAAGA 1140

TGGCTCTTAG CAAAGTCAAG TTGAATGATA CATTAAATAA GGATCAGCTG CTGTCATCCA 1200

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TCACAGGATT AATAGGTATG TTATATGCTA TGTCCAGGTT AGGAAGGGAA GACACTATAA 1380

AGATACTTAA AGATGCTGGA TATCATGTTA AAGCTAATGG AGTAGATATA ACAACATATC 1440

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TACCAAAGGA TATAGCTAAC AGTTTTTATG AAGTGTTTGA AAAACACCCT CATCTTATAG 1800

ATGTTTTCGT GCACTTTGGC ATTGCACAAT CATCCACAAG AGGGGGTAGT AGAGTTGAAG 1860

GAATCTTTGC AGGATTGTTT ATGAATGCCT ATGGTTCAGG GCAAGTAATG CTAAGATGGG 1920

GAGTTTTAGC CAAATCTGTA AAAAATATCA TGCTAGGACA TGCTAGTGTC CAGGCAGAAA 1980

TGGAGCAAGT TGTGGAAGTC TATGAGTATG CACAGAAGTT GGGAGGAGAA GCTGGATTCT 2040

ACCATATATT GAACAATCCA AAAGCATCAT TGCTGTCATT AACTCAATTT CCCAACTTCT 2100

CAAGTGTGGT CCTAGGCAAT GCAGCAGGTC TAGGCATAAT GGGAGAGTAT AGAGGTACAC 2160

CAAGAAACCA GGATCTTTAT GATGCAGCTA AAGCATATGC AGAGCAACTC AAAGAAAATG 2220

GAGTAATAAA CTACAGTGTA TTAGACTTAA CAGCAGAAGA ATTGGAAGCC ATAAAGCATC 2280

AACTCAACCC CAAAGAAGAT GATGTAGAGC TTTAAGTTAA CAAAAAATAC GGGGCAAATA 2340

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TAGGAATGAG GAAAGCGAAA AAATGGCAAA AGACACCTCA GATGAAGTGT CTCTTAATCC 3000

AACTTCCAAA AAATTGAGTG ACTTGTTGGA AGACAACGAT AGTGACAATG ATCTATCACT 3060

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AATATGGGTG CCTATGTTCC AGTCATCTGT GCCAGCAGAC TTGCTCATAA AAGAACTTGC 3420

AAGCATCAAT ATACTAGTGA AGCAGATCTC TACGCCCAAA GGACCTTCAC TACGAGTCAC 3480

GATTAACTCA AGAAGTGCTG TGCTGGCTCA AATGCCTAGT AATTTCATCA TAAGCGCAAA 3540

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AGCATGCAGT CTAACATGCT TAAAAGTAAA AAGTATGTTA ACTACAGTCA AAGATCTTAC 3660

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ACAATAGAAC TCACAAGCAA ATTTTGGCCC TATTTTACAC TAATACATAT GATCTTAACT 4380

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AGTTCCACCA TTATGCTGTG TCAAACCATA ATCCTGTATA TACAAACAAA CAAATCCAAT 4560

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GCCATAATAT TCATCATCTC TGCCAATCAC AAAGTTACAC TAACAACGGT CACAGTTCAA 4920

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AGGGTTAGTT CATCCAAGCA ACCCACAACC ACATCACCAA TCCACACAAG TTCAGCTACA 5040

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GCCAAAACGA CGAAAAAAGA AACTACCACC AACCCAACAA AAAAACTAAC CCTCAAGACC 5400

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TGTAACAATA AGCTATATTT AGATATATTG AAAGTATTAA AACACTTAAA AACTTTTTTT 11400

AATCTTGATA GCATTGATAT GGCTTTATCA TTGTATATGA ATTTGCCTAT GCTGTTTGGT 11460

GGTGGTGATC CTAATTTGTT ATATCGAAGC TTTTATAGGA GAACTCCAGA CTTCCTTACA 11520

GAAGCTATAG TACATTCAGT GTTTGTGTTG AGCTATTATA CTGGTCACGA TTTACAAGAT 11580

AAGCTCCAGG ATCTTCCAGA TGATAGACTG AACAAATTCT TGACATGTGT CATCACATTT 11640

GATAAAAATC CCAATGCCGA GTTTGTAACA TTGATGAGGG ATCCACAGGC TTTAGGGTCT 11700

GAAAGGCAAG CTAAAATTAC TAGTGAGATT AATAGATTAG CAGTAACAGA AGTCTTAAGT 11760

ATAGCCCCAA ACAAAATATT TTCTAAAAGT GCACAACATT ATACTACCAC TGAGATTGAT 11820

CTAAATGACA TTATGCAAAA TATAGAACCA ACTTACCCTC ATGGATTAAG AGTTGTTTAT 11880

GAAAGTTTAC CTTTTTATAA AGCAGAAAAA ATAGTTAATC TTATATCAGG AACAAAATCC 11940

ATAACTAATA TACTTGAAAA AACATCAGCA ATAGATACAA CTGATATTAA TAGGGCTACT 12000

GATATGATGA GGAAAAATAT AACTTTACTT ATAAGGATAC TTCCACTAGA TTGTAACAAA 12060

GACAAAAGAG AGTTATTAAG TTTAGAAAAT CTTAGTATAA CTGAATTAAG CAAGTATGTA 12120

AGAGAAAGAT CTTGGTCATT ATCCAATATA GTAGGAGTAA CATCGCCAAG TATTATGTTC 12180

ACAATGAACA TTAAATATAC AACTAGCACT ATAGCCAGTG GTATAATAAT AGAAAAATAT 12240

AATGTTAATA GTTTAACTCG TGGTGAAAGA GGACCCACCA AGCCATGGGT AGGCTCATCC 12300

ACGCAGGAGA AAAAAACAAT GCCAGTGTAC AACAGACAAG TTTTAACCAA AAAGCAAAGA 12360

GACCAAATAG ATTTATTAGC AAAATTAGAC TGGGTATATG CATCCATAGA CAACAAAGAT 12420

GAATTCATGG AAGAACTGAG TACTGGAACA CTTGGACTGT CATATGAAAA AGCCAAAAAG 12480

TTGTTTCCAC AATATCTAAG TGTCAATTAT TTACACCGTT TAACAGTCAG TAGTAGACCA 12540

TGTGAATTCC CTGCATCAAT ACCAGCTTAT AGAACAACAA ATTATCATTT TGATACTAGT 12600

CCTATCAATC ATGTATTAAC AGAAAAGTAT GGAGATGAAG ATATCGACAT TGTGTTTCAA 12660

AATTGCATAA GTTTTGGTCT TAGCCTGATG TCGGTTGTGG AACAATTCAC AAACATATGT 12720

CCTAATAGAA TTATTCTCAT ACCGAAGCTG AATGAGATAC ATTTGATGAA ACCTCCTATA 12780

TTTACAGGAG ATGTTGATAT CATCAAGTTG AAGCAAGTGA TACAAAAGCA GCACATGTTC 12840

CTACCAGATA AAATAAGTTT AACCCAATAT GTAGAATTAT TCTTAAGTAA CAAAGCACTT 12900

AAATCTGGAT CTCACATCAA CTCTAATTTA ATATTAGTAC ATAAAATGTC TGATTATTTT 12960

CATAATGCTT ATATTTTAAG TACTAATTTA GCTGGACATT GGATTCTGAT TATTCAACTT 13020

ATGAAAGATT CAAAAGGTAT TTTTGAAAAA GATTGGGGAG AGGGGTACAT AACTGATCAT 13080
ATGTTCATTA ATTTGAATGT TTTCTTTAAT GCTTATAAGA CTTATTTGCT ATGTTTTCAT 13140
AAAGGTTATG GTAAAGCAAA ATTAGAATGT GATATGAACA CTTCAGATCT TCTTTGTGTT 13200
TTGGAGTTAA TAGACAGTAG CTACTGGAAA TCTATGTCTA AAGTTTTCCT AGAACAAAAA 13260
GTCATAAAAT ACATAGTCAA TCAAGACACA AGTTTGCGTA GAATAAAAGG CTGTCACAGT 13320
TTTAAGTTGT GGTTTTTAAA ACGCCTTAAT AATGCTAAAT TTACCGTATG CCCTTGGGTT 13380
GTTAACATAG ATTATCACCC AACACACATG AAAGCTATAT TATCTTACAT AGATTTAGTT 13440
AGAATGGGGT TAATAAATGT AGATAAATTA ACCATTAAAA ATAAAAACAA ATTCAATGAT 13500
GAATTTTACA CATCAAATCT CTTTTACATT AGTTATAACT TTTCAGACAA CACTCATTTG 13560
CTAACAAAAC AAATAAGAAT TGCTAATTCA GAATTAGAAG ATAATTATAA CAAACTATAT 13620
CACCCAACCC CAGAAACTTT AGAAAATATG TCATTAATTC CTGTTAAAAG TAATAATAGT 13680
AACAAACCTA AATTTTGTAT AAGTGGAAAT ACCGAATCTA TGATGATGTC AACATTCTCT 13740
AGTAAAATGC ATATTAAATC TTCCACTGTT ACCACAAGAT TCAATTATAG CAAACAAGAC 13800
TTGTACAATT TATTTCCAAT TGTTGTGATA GACAAGATTA TAGATCATTC AGGTAATACA 13860
GCAAAATCTA ACCAACTTTA CACCACCACT TCACATCAGA CATCTTTAGT AAGGAATAGT 13920
GCATCACTTT ATTGCATGCT TCCTTGGCAT CATGTCAATA GATTTAACTT TGTATTTAGT 13980
TCCACAGGAT GCAAGATCAG TATAGAGTAT ATTTTAAAAG ATCTTAAGAT TAAGGACCCC 14040
AGTTGTATAG CATTCATAGG TGAAGGAGCT GGTAACTTAT TATTACGTAC GGTAGTAGAA 14100
CTTCATCCAG ACATAAGATA CATTTACAGA AGTTTAAAAG ATTGCAATGA TCATAGTTTA 14160
CCTATTGAAT TTCTAAGGTT ATACAACGGG CATATAAACA TAGATTATGG TGAGAATTTA 14220
ACCATTCCTG CTACAGATGC AACTAATAAC ATTCATTGGT CTTATTTACA TATAAAATTT 14280
GCAGAACCTA TTAGCATCTT TGTCTGCGAT GCTGAATTAC CTGTTACAGC CAATTGGAGT 14340
AAAATTATAA TTGAATGGAG TAAGCATGTA AGAAAGTGCA AGTACTGTTC TTCTGTAAAT 14400
AGATGCATTT TAATTGCAAA ATATCATGCT CAAGATGACA TTGATTTCAA ATTAGATAAC 14460
ATTACTATAT TAAAAACTTA CGTGTGCCTA GGTAGCAAGT TAAAAGGATC TGAAGTTTAC 14520
TTAATCCTTA CAATAGGCCC TGCAAATATA CTTCCTGTTT TTGATGTTGT ACAAAATGCT 14580

AAATTGATAC TTTCAAGAAC TAAAAATTTC ATTATGCCTA AAAAAACTGA CAAGGAATCT 14640

ATCGATGCAA ATATTAAAAG CTTAATACCT TTCCTTTGTT ACCCTATAAC AAAAAAAGGA 14700

ATTAAGACTT CATTGTCAAA ATTGAAGAGT GTAGTTAATG GAGATATATT ATCATATTCT 14760

ATAGCTGGAC GTAATGAAGT ATTCAGCAAC AAGCTTATAA ACCACAAGCA TATGAATATC 14820

CTAAAATGGC TAGATCATGT TTTAAATTTT AGATCAGCTG AACTTAATTA CAATCATTTA 14880

TACATGATAG AGTCCACATA TCCTTACTTA AGTGAATTGT TAAATAGTTT AACAACCAAT 14940

GAGCTCAAGA AGCTGATTAA AATAACAGGT AGTGTGCTAT ACAACCTTCC CAACGAACAG 15000

TAGTTTAAAA TATCATTAAC AAGTTTGGTC AAATTTAGAT GCTAACACAT CATTATATTA 15060

TAGTTATTAA AGAATATACA AACTTTTCAA TAATTTAGCA TATTGATTCC AAAATTATCA 15120

TTTTAGTCTT AAGGGGTTAA ATAAAAGTCT AAAACTAACA ATTATACATG TGCATTCACA 15180

ACACAACGAG ACATTAGTTT TTGACACTTT TTTTCTCGT 15219

(2) INFORMATION FOR SEQ ID NO:28:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2166 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:28:

Met Asp Pro Ile Ile Asn Gly Asn Ser Ala Asn Val Tyr Leu Thr Asp
1 5 10 15

Ser Tyr Leu Lys Gly Val Ile Ser Phe Ser Glu Cys Asn Ala Leu Gly
20 25 30

Ser Tyr Leu Phe Asn Gly Pro Tyr Leu Lys Asn Asp Tyr Thr Asn Leu
35 40 45

Ile Ser Arg Gln Ser Pro Leu Leu Glu His Met Asn Leu Lys Lys Leu
50 55 60

Thr Ile Thr Gln Ser Leu Ile Ser Arg Tyr His Lys Gly Glu Leu Lys
65 70 75 80

Leu Glu Glu Pro Thr Tyr Phe Gln Ser Leu Leu Met Thr Tyr Lys Ser
85 90 95

Met Ser Ser Ser Glu Gln Ile Ala Thr Thr Asn Leu Leu Lys Lys Ile
100 105 110

Ile Arg Arg Ala Ile Glu Ile Ser Asp Val Lys Val Tyr Ala Ile Leu
115 120 125

Asn Lys Leu Gly Leu Lys Glu Lys Asp Arg Val Lys Pro Asn Asn Asn
130 135 140

Ser Gly Asp Glu Asn Ser Val Leu Thr Thr Ile Ile Lys Asp Asp Ile
145 150 155 160

Leu Ser Ala Val Glu Asn Asn Gln Ser Tyr Thr Asn Ser Asp Lys Ser
165 170 175

His Ser Val Asn Gln Asn Ile Thr Ile Lys Thr Thr Leu Leu Lys Lys
180 185 190

Leu Met Cys Ser Met Gln His Pro Pro Ser Trp Leu Ile His Trp Phe
195 200 205

Asn Leu Tyr Thr Lys Leu Asn Asn Ile Leu Thr Gln Tyr Arg Ser Asn
210 215 220

Glu Val Lys Ser His Gly Phe Ile Leu Ile Asp Asn Gln Thr Leu Ser
225 230 235 240

Gly Phe Gln Phe Ile Leu Asn Gln Tyr Gly Cys Ile Val Tyr His Lys
245 250 255

Gly Leu Lys Lys Ile Thr Thr Thr Thr Tyr Asn Gln Phe Leu Thr Trp
260 265 270

Lys Asp Ile Ser Leu Ser Arg Leu Asn Val Cys Leu Ile Thr Trp Ile
275 280 285

Ser Asn Cys Leu Asn Thr Leu Asn Lys Ser Leu Gly Leu Arg Cys Gly
290 295 300

Phe Asn Asn Val Val Leu Ser Gln Leu Phe Leu Tyr Gly Asp Cys Ile
305 310 315 320

Leu Lys Leu Phe His Asn Glu Gly Phe Tyr Ile Ile Lys Glu Val Glu
325 330 335

Gly Phe Ile Met Ser Leu Ile Leu Asn Ile Thr Glu Glu Asp Gln Phe
340 345 350

Lys Lys Arg Phe Tyr Asn Ser Met Leu Asn Asn Ile Thr Asp Ala Ala
355 360 365

Ile Lys Ala Gln Lys Asp Leu Leu Ser Arg Val Cys His Thr Leu Leu
370 375 380

Asp Lys Thr Val Ser Asp Asn Ile Ile Asn Gly Lys Trp Ile Ile Leu
385 390 395 400

Leu Ser Lys Phe Leu Lys Leu Ile Lys Leu Ala Gly Asp Asn Asn Leu
405 410 415

Asn Asn Leu Ser Glu Leu Tyr Phe Leu Phe Arg Ile Phe Gly His Pro
420 425 430

Met Val Asp Glu Arg Gln Ala Met Asp Ser Val Arg Ile Asn Cys Asn
435 440 445

Glu Thr Arg Phe Tyr Leu Leu Ser Ser Leu Ser Thr Leu Arg Gly Ala
450 455 460

Phe Ile Tyr Arg Ile Ile Lys Gly Phe Val Asn Thr Tyr Asn Arg Trp
465 470 475 480

Pro Thr Leu Arg Asn Ala Ile Val Leu Pro Leu Arg Trp Leu Asn Tyr
485 490 495

Tyr Lys Leu Asn Thr Tyr Pro Ser Leu Leu Glu Ile Thr Glu Asn Asp
500 505 510

Leu Ile Ile Leu Ser Gly Leu Arg Phe Tyr Arg Glu Phe His Leu Pro
515 520 525

Lys Lys Val Asp Leu Glu Met Ile Ile Asn Asp Lys Ala Ile Ser Pro
530 535 540

Pro Lys Asp Leu Ile Trp Thr Ser Phe Pro Arg Asn Tyr Met Pro Ser
545 550 555 560

His Ile Gln Asn Tyr Ile Glu His Glu Lys Leu Lys Phe Ser Glu Ser
565 570 575

Asp Arg Ser Arg Arg Val Leu Glu Tyr Tyr Leu Arg Asp Asn Lys Phe
580 585 590

Asn Glu Cys Asp Leu Tyr Asn Cys Val Val Asn Gln Ser Tyr Leu Asn
595 600 605

Asn Ser Asn His Val Val Ser Leu Thr Gly Lys Glu Arg Glu Leu Ser
610 615 620

Val Gly Arg Met Phe Ala Met Gln Pro Gly Met Phe Arg Gln Ile Gln

625 630 635 640

Ile Leu Ala Glu Lys Met Ile Ala Glu Asn Ile Leu Gln Phe Phe Pro
645 650 655

Glu Ser Leu Thr Arg Tyr Gly Asp Leu Glu Leu Gln Lys Ile Leu Glu
660 665 670

Leu Lys Ala Gly Ile Ser Asn Lys Ser Asn Arg Tyr Asn Asp Asn Tyr
675 680 685

Asn Asn Tyr Ile Ser Lys Cys Ser Ile Ile Thr Asp Leu Ser Lys Phe
690 695 700

Asn Gln Ala Phe Arg Tyr Glu Thr Ser Cys Ile Cys Ser Asp Val Leu
705 710 715 720

Asp Glu Leu His Gly Val Gln Ser Leu Phe Ser Trp Leu His Leu Thr
725 730 735

Ile Pro Leu Val Thr Ile Ile Cys Thr Tyr Arg His Ala Pro Pro Phe
740 745 750

Ile Lys Asp His Val Val Asn Leu Asn Glu Val Asp Glu Gln Ser Gly
755 760 765

Leu Tyr Arg Tyr His Met Gly Gly Ile Glu Gly Trp Cys Gln Lys Leu
770 775 780

Trp Thr Ile Glu Ala Ile Ser Leu Leu Asp Leu Ile Ser Leu Lys Gly
785 790 795 800

Lys Phe Ser Ile Thr Ala Leu Ile Asn Gly Asp Asn Gln Ser Ile Asp
805 810 815

Ile Ser Lys Pro Val Arg Leu Ile Glu Gly Gln Thr His Ala Gln Ala
820 825 830

Asp Tyr Leu Leu Ala Leu Asn Ser Leu Lys Leu Leu Tyr Lys Glu Tyr
835 840 845

Ala Gly Ile Gly His Lys Leu Lys Gly Thr Glu Thr Tyr Ile Ser Arg
850 855 860

Asp Met Gln Phe Met Ser Lys Thr Ile Gln His Asn Gly Val Tyr Tyr
865 870 875 880

Pro Ala Ser Ile Lys Lys Val Leu Arg Val Gly Pro Trp Ile Asn Thr
885 890 895

Ile Leu Asp Asp Phe Lys Val Ser Leu Glu Ser Ile Gly Ser Leu Thr
900 905 910

Gln Glu Leu Glu Tyr Arg Gly Glu Ser Leu Leu Cys Ser Leu Ile Phe
915 920 925

Arg Asn Ile Trp Leu Tyr Asn Gln Ile Ala Leu Gln Leu Arg Asn His
930 935 940

Ala Leu Cys Asn Asn Lys Leu Tyr Leu Asp Ile Leu Lys Val Leu Lys
945 950 955 960

His Leu Lys Thr Phe Phe Asn Leu Asp Ser Ile Asp Met Ala Leu Ser
965 970 975

Leu Tyr Met Asn Leu Pro Met Leu Phe Gly Gly Gly Asp Pro Asn Leu
980 985 990

Leu Tyr Arg Ser Phe Tyr Arg Arg Thr Pro Asp Phe Leu Thr Glu Ala
995 1000 1005

Ile Val His Ser Val Phe Val Leu Ser Tyr Tyr Thr Gly His Asp Leu
1010 1015 1020

Gln Asp Lys Leu Gln Asp Leu Pro Asp Asp Arg Leu Asn Lys Phe Leu
1025 1030 1035 1040

Thr Cys Val Ile Thr Phe Asp Lys Asn Pro Asn Ala Glu Phe Val Thr
1045 1050 1055

Leu Met Arg Asp Pro Gln Ala Leu Gly Ser Glu Arg Gln Ala Lys Ile
1060 1065 1070

Thr Ser Glu Ile Asn Arg Leu Ala Val Thr Glu Val Leu Ser Ile Ala
1075 1080 1085

Pro Asn Lys Ile Phe Ser Lys Ser Ala Gln His Tyr Thr Thr Thr Glu
1090 1095 1100

Ile Asp Leu Asn Asp Ile Met Gln Asn Ile Glu Pro Thr Tyr Pro His
1105 1110 1115 1120

Gly Leu Arg Val Val Tyr Glu Ser Leu Pro Phe Tyr Lys Ala Glu Lys
1125 1130 1135

Ile Val Asn Leu Ile Ser Gly Thr Lys Ser Ile Thr Asn Ile Leu Glu
1140 1145 1150

Lys Thr Ser Ala Ile Asp Thr Thr Asp Ile Asn Arg Ala Thr Asp Met
1155 1160 1165

Met Arg Lys Asn Ile Thr Leu Leu Ile Arg Ile Leu Pro Leu Asp Cys
1170 1175 1180

Asn Lys Asp Lys Arg Glu Leu Leu Ser Leu Glu Asn Leu Ser Ile Thr
1185 1190 1195 1200

Glu Leu Ser Lys Tyr Val Arg Glu Arg Ser Trp Ser Leu Ser Asn Ile
1205 1210 1215

Val Gly Val Thr Ser Pro Ser Ile Met Phe Thr Met Asn Ile Lys Tyr
1220 1225 1230

Thr Thr Ser Thr Ile Ala Ser Gly Ile Ile Ile Glu Lys Tyr Asn Val
1235 1240 1245

Asn Ser Leu Thr Arg Gly Glu Arg Gly Pro Thr Lys Pro Trp Val Gly
1250 1255 1260

Ser Ser Thr Gln Glu Lys Lys Thr Met Pro Val Tyr Asn Arg Gln Val
1265 1270 1275 1280

Leu Thr Lys Lys Gln Arg Asp Gln Ile Asp Leu Leu Ala Lys Leu Asp
1285 1290 1295

Trp Val Tyr Ala Ser Ile Asp Asn Lys Asp Glu Phe Met Glu Glu Leu
1300 1305 1310

Ser Thr Gly Thr Leu Gly Leu Ser Tyr Glu Lys Ala Lys Lys Leu Phe
1315 1320 1325

Pro Gln Tyr Leu Ser Val Asn Tyr Leu His Arg Leu Thr Val Ser Ser
1330 1335 1340

Arg Pro Cys Glu Phe Pro Ala Ser Ile Pro Ala Tyr Arg Thr Thr Asn
1345 1350 1355 1360

Tyr His Phe Asp Thr Ser Pro Ile Asn His Val Leu Thr Glu Lys Tyr
1365 1370 1375

Gly Asp Glu Asp Ile Asp Ile Val Phe Gln Asn Cys Ile Ser Phe Gly
1380 1385 1390

Leu Ser Leu Met Ser Val Val Glu Gln Phe Thr Asn Ile Cys Pro Asn
1395 1400 1405

Arg Ile Ile Leu Ile Pro Lys Leu Asn Glu Ile His Leu Met Lys Pro
1410 1415 1420

Pro Ile Phe Thr Gly Asp Val Asp Ile Ile Lys Leu Lys Gln Val Ile
1425 1430 1435 1440

Gln Lys Gln His Met Phe Leu Pro Asp Lys Ile Ser Leu Thr Gln Tyr
1445 1450 1455

Val Glu Leu Phe Leu Ser Asn Lys Ala Leu Lys Ser Gly Ser His Ile

1460 1465 1470

Asn Ser Asn Leu Ile Leu Val His Lys Met Ser Asp Tyr Phe His Asn
1475 1480 1485

Ala Tyr Ile Leu Ser Thr Asn Leu Ala Gly His Trp Ile Leu Ile Ile
1490 1495 1500

Gln Leu Met Lys Asp Ser Lys Gly Ile Phe Glu Lys Asp Trp Gly Glu
1505 1510 1515 1520

Gly Tyr Ile Thr Asp His Met Phe Ile Asn Leu Asn Val Phe Phe Asn
1525 1530 1535

Ala Tyr Lys Thr Tyr Leu Leu Cys Phe His Lys Gly Tyr Gly Lys Ala
1540 1545 1550

Lys Leu Glu Cys Asp Met Asn Thr Ser Asp Leu Leu Cys Val Leu Glu
1555 1560 1565

Leu Ile Asp Ser Ser Tyr Trp Lys Ser Met Ser Lys Val Phe Leu Glu
1570 1575 1580

Gln Lys Val Ile Lys Tyr Ile Val Asn Gln Asp Thr Ser Leu Arg Arg
1585 1590 1595 1600

Ile Lys Gly Cys His Ser Phe Lys Leu Trp Phe Leu Lys Arg Leu Asn
1605 1610 1615

Asn Ala Lys Phe Thr Val Cys Pro Trp Val Val Asn Ile Asp Tyr His
1620 1625 1630

Pro Thr His Met Lys Ala Ile Leu Ser Tyr Ile Asp Leu Val Arg Met
1635 1640 1645

Gly Leu Ile Asn Val Asp Lys Leu Thr Ile Lys Asn Lys Asn Lys Phe
1650 1655 1660

Asn Asp Glu Phe Tyr Thr Ser Asn Leu Phe Tyr Ile Ser Tyr Asn Phe
1665 1670 1675 1680

Ser Asp Asn Thr His Leu Leu Thr Lys Gln Ile Arg Ile Ala Asn Ser
1685 1690 1695

Glu Leu Glu Asp Asn Tyr Asn Lys Leu Tyr His Pro Thr Pro Glu Thr
1700 1705 1710

Leu Glu Asn Met Ser Leu Ile Pro Val Lys Ser Asn Asn Ser Asn Lys
1715 1720 1725

Pro Lys Phe Cys Ile Ser Gly Asn Thr Glu Ser Met Met Met Ser Thr
1730 1735 1740

Phe Ser Ser Lys Met His Ile Lys Ser Ser Thr Val Thr Thr Arg Phe
1745 1750 1755 1760

Asn Tyr Ser Lys Gln Asp Leu Tyr Asn Leu Phe Pro Ile Val Val Ile
1765 1770 1775

Asp Lys Ile Ile Asp His Ser Gly Asn Thr Ala Lys Ser Asn Gln Leu
1780 1785 1790

Tyr Thr Thr Thr Ser His Gln Thr Ser Leu Val Arg Asn Ser Ala Ser
1795 1800 1805

Leu Tyr Cys Met Leu Pro Trp His His Val Asn Arg Phe Asn Phe Val
1810 1815 1820

Phe Ser Ser Thr Gly Cys Lys Ile Ser Ile Glu Tyr Ile Leu Lys Asp
1825 1830 1835 1840

Leu Lys Ile Lys Asp Pro Ser Cys Ile Ala Phe Ile Gly Glu Gly Ala
1845 1850 1855

Gly Asn Leu Leu Leu Arg Thr Val Val Glu Leu His Pro Asp Ile Arg
1860 1865 1870

Tyr Ile Tyr Arg Ser Leu Lys Asp Cys Asn Asp His Ser Leu Pro Ile
1875 1880 1885

Glu Phe Leu Arg Leu Tyr Asn Gly His Ile Asn Ile Asp Tyr Gly Glu
1890 1895 1900

Asn Leu Thr Ile Pro Ala Thr Asp Ala Thr Asn Asn Ile His Trp Ser
1905 1910 1915 1920

Tyr Leu His Ile Lys Phe Ala Glu Pro Ile Ser Ile Phe Val Cys Asp
1925 1930 1935

Ala Glu Leu Pro Val Thr Ala Asn Trp Ser Lys Ile Ile Ile Glu Trp
1940 1945 1950

Ser Lys His Val Arg Lys Cys Lys Tyr Cys Ser Ser Val Asn Arg Cys
1955 1960 1965

Ile Leu Ile Ala Lys Tyr His Ala Gln Asp Asp Ile Asp Phe Lys Leu
1970 1975 1980

Asp Asn Ile Thr Ile Leu Lys Thr Tyr Val Cys Leu Gly Ser Lys Leu
1985 1990 1995 2000

Lys Gly Ser Glu Val Tyr Leu Ile Leu Thr Ile Gly Pro Ala Asn Ile
2005 2010 2015

Leu Pro Val Phe Asp Val Val Gln Asn Ala Lys Leu Ile Leu Ser Arg
2020 2025 2030

Thr Lys Asn Phe Ile Met Pro Lys Lys Thr Asp Lys Glu Ser Ile Asp
2035 2040 2045

Ala Asn Ile Lys Ser Leu Ile Pro Phe Leu Cys Tyr Pro Ile Thr Lys
2050 2055 2060

Lys Gly Ile Lys Thr Ser Leu Ser Lys Leu Lys Ser Val Val Asn Gly
2065 2070 2075 2080

Asp Ile Leu Ser Tyr Ser Ile Ala Gly Arg Asn Glu Val Phe Ser Asn
2085 2090 2095

Lys Leu Ile Asn His Lys His Met Asn Ile Leu Lys Trp Leu Asp His
2100 2105 2110

Val Leu Asn Phe Arg Ser Ala Glu Leu Asn Tyr Asn His Leu Tyr Met
2115 2120 2125

Ile Glu Ser Thr Tyr Pro Tyr Leu Ser Glu Leu Leu Asn Ser Leu Thr
2130 2135 2140

Thr Asn Glu Leu Lys Lys Leu Ile Lys Ile Thr Gly Ser Val Leu Tyr
2145 2150 2155 2160

Asn Leu Pro Asn Glu Gln
2165

(2) INFORMATION FOR SEQ ID NO:29:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 15219 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:29:

ACGGGAAAAA AATGCGTACT ACAAACTTGC ACATTCGAAA AAAATGGGGC AAATAAGAAC 60

TTGATAAGTG CTATTTAAGT CTAACCTTTT CAATCAGAAA TGGGGTGCAA TTCACTGAGC 120

ATGATAAAGG TTAGATTACA AAATTTATTT GACAATGACG AAGTAGCATT GTTAAAAATA 180

ACATGTTATA CTGATAAATT AATTCTTCTG ACCAATGCAT TAGCCAAAGC AGCAATACAT 240

ACAATTAAAT TAAACGGCAT AGTTTTTATA CATGTTATAA CAAGCAGTGA AGTGTGCCCT 300

GATAACAATA TTGTAGTGAA ATCTAACTTT ACAACAATGC CAATACTACA AAATGGAGGA 360

TACATATGGG AATTGATTGA GTTGACACAC TGCTCTCAAT TAAACGGTTT AATGGATGAT 420

AATTGTGAAA TCAAATTTTC TAAAAGACTA AGTGACTCAG TAATGACTAA TTATATGAAT 480

CAAATATCTG ACTTACTTGG GCTTGATCTC AATTCATGAA TTATGTTTAG TCTAATTCAA 540

TAGACATGTG TTTATTACCA TTTTAGTTAA TATAAAAACT CATCAAAGGG AAATGGGGCA 600

AATAAACTCA CCTAATCAAT CAAACCATGA GCACTACAAA TGACAACACT ACTATGCAAA 660

GATTGATGAT CACAGACATG AGACCCCTGT CAATGGATTC AATAATAACA TCTCTTACCA 720

AAGAAATCAT CACACACAAA TTCATATACT TGATAAACAA TGAATGTATT GTAAGAAAAC 780

TTGATGAAAG ACAAGCTACA TTTACATTCT TAGTCAATTA TGAGATGAAG CTACTGCACA 840

AAGTAGGGAG TACCAAATAC AAAAAATACA CTGAATATAA TACAAAATAT GGCACTTTCC 900

CCATGCCTAT ATTTATCAAT CACGGCGGGT TTCTAGAATG TATTGGCATT AAGCCTACAA 960

AACACACTCC TATAATATAC AAATATGACC TCAACCCGTG AATTCCAACA AAAAAACCAA 1020

CCCAACCAAA CCAAACTATT CCTCAAACAA CAGTGCTCAA TAGTTAAGAA GGAGCTAATC 1080

CATTTTAGTA ATTAAAAATA AAAGTAAAGC CAATAACATA AATTGGGGCA AATACAAAGA 1140

TGGCTCTTAG CAAAGTCAAG TTGAATGATA CATTAAATAA GGATCAGCTG CTGTCATCCA 1200

GCAAATACAC TATTCAACGT AGTACAGGAG ATAATATTGA CACTCCCAAT TATGATGTGC 1260

AAAAACACCT AAACAAACTA TGTGGTATGC TATTAATCAC TGAAGATGCA AATCATAAAT 1320

TCACAGGATT AATAGGTATG TTATATGCTA TGTCCAGGTT AGGAAGGGAA GACACTATAA 1380

AGATACTTAA AGATGCTGGA TATCATGTTA AAGCTAATGG AGTAGATATA ACAACATATC 1440

GTCAAGATAT AAATGGAAAG GAAATGAAAT TCGAAGTATT AACATTATCA AGCTTGACAT 1500

CAGAAATACA AGTCAATATT GAGATAGAAT CTAGAAAGTC CTACAAAAAA ATGCTAAAAG 1560

AGATGGGAGA AGTGGCTCCA GAATATAGGC ATGATTCTCC AGACTGTGGG ATGATAATAC 1620

TGTGTATAGC TGCACTTGTG ATAACCAAAT TAGCAGCAGG AGACAGATCA GGTCTTACAG 1680

CAGTAATTAG GAGGGCAAAC AATGTCTTAA AAAACGAAAT AAAACGATAC AAGGGCCTCA 1740

TACCAAAGGA TATAGCTAAC AGTTTTTATG AAGTGTTTGA AAAACACCCT CATCTTATAG 1800

ATGTTTTCGT GCACTTTGGC ATTGCACAAT CATCCACAAG AGGGGGTAGT AGAGTTGAAG 1860

GAATCTTTGC AGGATTGTTT ATGAATGCCT ATGGTTCAGG GCAAGTAATG CTAAGATGGG 1920

GAGTTTTAGC CAAATCTGTA AAAAATATCA TGCTAGGACA TGCTAGTGTC CAGGCAGAAA 1980

TGGAGCAAGT TGTGGAAGTC TATGAGTATG CACAGAAGTT GGGAGGAGAA GCTGGATTCT 2040

ACCATATATT GAACAATCCA AAAGCATCAT TGCTGTCATT AACTCAATTT CCCAACTTCT 2100

CAAGTGTGGT CCTAGGCAAT GCAGCAGGTC TAGGCATAAT GGGAGAGTAT AGAGGTACAC 2160

CAAGAAACCA GGATCTTTAT GATGCAGCTA AAGCATATGC AGAGCAACTC AAAGAAAATG 2220

GAGTAATAAA CTACAGTGTA TTAGACTTAA CAGCAGAAGA ATTGGAAGCC ATAAAGCATC 2280

AACTCAACCC CAAAGAAGAT GATGTAGAGC TTTAAGTTAA CAAAAAATAC GGGGCAAATA 2340

AGTCAACATG GAGAAGTTTG CACCTGAATT TCATGGAGAA GATGCAAATA ACAAAGCTAC 2400

CAAATTCCTA GAATCAATAA AGGGCAAGTT CGCATCATCC AAAGATCCTA AGAAGAAAGA 2460

TAGCATAATA TCTGTTAACT CAATAGATAT AGAAGTAACT AAAGAGAGCC CGATAACATC 2520

TGGCACCAAC ATCATCAATC CAACAAGTGA AGCCGACAGT ACCCCAGAAA CAAAAGCCAA 2580

CTACCCAAGA AAACCCCTAG TAAGCTTCAA AGAAGATCTC ACCCCAAGTG ACAACCCTTT 2640

TTCTAAGTTG TACAAGGAAA CAATAGAAAC ATTTGATAAC AATGAAGAAG AATCTAGCTA 2700

CTCATATGAA GAGATAAATG ATCAAACAAA TGACAACATT ACAGCAAGAC TAGATAGAAT 2760

TGATGAAAAA TTAAGTGAAA TATTAGGAAT GCTCCATACA TTAGTAGTTG CAAGTGCAGG 2820

ACCCACTTCA GCTCGCGATG GAATAAGAGA TGCTATGGTT GGTCTAAGAG AAGAGATGAT 2880

AGAAAAAATA AGAGCGGAAG CATTAATGAC CAATGATAGG TTAGAGGCTA TGGCAAGACT 2940

TAGGAATGAG GAAAGCGAAA AAATGGCAAA AGACACCTCA GATGAAGTGT CTCTTAATCC 3000

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ACACAACGAG ACATTAGTTT TTGACACTTT TTTTCTCGT 15219

(2) INFORMATION FOR SEQ ID NO:30:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2166 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:30:

Met Asp Pro Ile Ile Asn Gly Asn Ser Ala Asn Val Tyr Leu Thr Asp
1 5 10 15

Ser Tyr Leu Lys Gly Val Ile Ser Phe Ser Glu Cys Asn Ala Leu Gly

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        20                  25                  30

Ser Tyr Leu Phe Asn Gly Pro Tyr Leu Lys Asn Asp Tyr Thr Asn Leu
        35                  40                  45

Ile Ser Arg Gln Ser Pro Leu Leu Glu His Met Asn Leu Lys Lys Leu
    50                  55                  60

Thr Ile Thr Gln Ser Leu Ile Ser Arg Tyr His Lys Gly Glu Leu Lys
65                  70                  75                  80

Leu Glu Glu Pro Thr Tyr Phe Gln Ser Leu Leu Met Thr Tyr Lys Ser
                85                  90                  95

Met Ser Ser Ser Glu Gln Ile Ala Thr Thr Asn Leu Leu Lys Lys Ile
            100                 105                 110

Ile Arg Arg Ala Ile Glu Ile Ser Asp Val Lys Val Tyr Ala Ile Leu
        115                 120                 125

Asn Lys Leu Gly Leu Lys Glu Lys Asp Arg Val Lys Pro Asn Asn Asn
    130                 135                 140

Ser Gly Asp Glu Asn Ser Val Leu Thr Thr Ile Ile Lys Asp Asp Ile
145                 150                 155                 160

Leu Ser Ala Val Glu Asn Asn Gln Ser Tyr Thr Asn Ser Asp Lys Ser
                165                 170                 175

His Ser Val Asn Gln Asn Ile Thr Ile Lys Thr Thr Leu Leu Lys Lys
            180                 185                 190

Leu Met Cys Ser Met Gln His Pro Pro Ser Trp Leu Ile His Trp Phe
        195                 200                 205

Asn Leu Tyr Thr Lys Leu Asn Asn Ile Leu Thr Gln Tyr Arg Ser Asn
    210                 215                 220

Glu Val Lys Ser His Gly Phe Ile Leu Ile Asp Asn Gln Thr Leu Ser
225                 230                 235                 240

Gly Phe Gln Phe Ile Leu Asn Gln Tyr Gly Cys Ile Val Tyr His Lys
                245                 250                 255

Gly Leu Lys Lys Ile Thr Thr Thr Thr Tyr Asn Gln Phe Leu Thr Trp
            260                 265                 270

Lys Asp Ile Ser Leu Ser Arg Leu Asn Val Cys Leu Ile Thr Trp Ile
        275                 280                 285

Ser Asn Cys Leu Asn Thr Leu Asn Lys Ser Leu Gly Leu Arg Cys Gly
    290                 295                 300
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Phe Asn Asn Val Val Leu Ser Gln Leu Phe Leu Tyr Gly Asp Cys Ile
305 310 315 320

Leu Lys Leu Phe His Asn Glu Gly Phe Tyr Ile Ile Lys Glu Val Glu
325 330 335

Gly Phe Ile Met Ser Leu Ile Leu Asn Ile Thr Glu Glu Asp Gln Phe
340 345 350

Arg Lys Arg Phe Tyr Asn Ser Met Leu Asn Asn Ile Thr Asp Ala Ala
355 360 365

Ile Lys Ala Gln Lys Asp Leu Leu Ser Arg Val Cys His Thr Leu Leu
370 375 380

Asp Lys Thr Val Ser Asp Asn Ile Ile Asn Gly Lys Trp Ile Ile Leu
385 390 395 400

Leu Ser Lys Phe Leu Lys Leu Ile Lys Leu Ala Gly Asp Asn Asn Leu
405 410 415

Asn Asn Leu Ser Glu Leu Tyr Phe Leu Phe Arg Ile Phe Gly His Pro
420 425 430

Met Val Asp Glu Arg Gln Ala Met Asp Ser Val Arg Ile Asn Cys Asn
435 440 445

Glu Thr Lys Phe Tyr Leu Leu Ser Ser Leu Ser Thr Leu Arg Gly Ala
450 455 460

Phe Ile Tyr Arg Ile Ile Lys Gly Phe Val Asn Thr Tyr Asn Arg Trp
465 470 475 480

Pro Thr Leu Arg Asn Ala Ile Val Leu Pro Leu Arg Trp Leu Asn Tyr
485 490 495

Tyr Lys Leu Asn Thr Tyr Pro Ser Leu Leu Glu Ile Thr Glu Asn Asp
500 505 510

Leu Ile Ile Leu Ser Gly Leu Arg Phe Tyr Arg Glu Phe His Leu Pro
515 520 525

Lys Lys Val Asp Leu Glu Met Ile Ile Asn Asp Lys Ala Ile Ser Pro
530 535 540

Pro Lys Asp Leu Ile Trp Thr Ser Phe Pro Arg Asn Tyr Met Pro Ser
545 550 555 560

His Ile Gln Asn Tyr Ile Glu His Glu Lys Leu Lys Phe Ser Glu Ser
565 570 575

Asp Arg Ser Arg Arg Val Leu Glu Tyr Tyr Leu Arg Asp Asn Lys Phe
580 585 590

Asn Glu Cys Asp Leu Tyr Asn Cys Val Val Asn Gln Ser Tyr Leu Asn
595 600 605

Asn Ser Asn His Val Val Ser Leu Thr Gly Lys Glu Arg Glu Leu Ser
610 615 620

Val Gly Arg Met Phe Ala Met Gln Pro Gly Met Phe Arg Gln Ile Gln
625 630 635 640

Ile Leu Ala Glu Lys Met Ile Ala Glu Asn Ile Leu Gln Phe Phe Pro
645 650 655

Glu Ser Leu Thr Arg Tyr Gly Asp Leu Glu Leu Gln Lys Ile Leu Glu
660 665 670

Leu Lys Ala Gly Ile Ser Asn Lys Ser Asn Arg Tyr Asn Asp Asn Tyr
675 680 685

Asn Asn Tyr Ile Ser Lys Cys Ser Ile Ile Thr Asp Leu Ser Lys Phe
690 695 700

Asn Gln Ala Phe Arg Tyr Glu Thr Ser Cys Ile Cys Ser Asp Val Leu
705 710 715 720

Asp Glu Leu His Gly Val Gln Ser Leu Phe Ser Trp Leu His Leu Thr
725 730 735

Ile Pro Leu Val Thr Ile Ile Cys Thr Tyr Arg His Ala Pro Pro Phe
740 745 750

Ile Lys Asp His Val Val Asn Leu Asn Glu Val Asp Glu Gln Ser Gly
755 760 765

Leu Tyr Arg Tyr His Met Gly Gly Ile Glu Gly Trp Cys Gln Lys Leu
770 775 780

Trp Thr Ile Glu Ala Ile Ser Leu Leu Asp Leu Ile Ser Leu Lys Gly
785 790 795 800

Lys Phe Ser Ile Thr Ala Leu Ile Asn Gly Asp Asn Gln Ser Ile Asp
805 810 815

Ile Ser Lys Pro Val Arg Leu Ile Glu Gly Gln Thr His Ala Gln Ala
820 825 830

Asp Tyr Leu Leu Ala Leu Asn Ser Leu Lys Leu Leu Tyr Lys Glu Tyr
835 840 845

Ala Gly Ile Gly His Lys Leu Lys Gly Thr Glu Thr Tyr Ile Ser Arg

850 855 860

Asp Met Gln Phe Met Ser Lys Thr Ile Gln His Asn Gly Val Tyr Tyr
865 870 875 880

Pro Ala Ser Ile Lys Lys Val Leu Arg Val Gly Pro Trp Ile Asn Thr
885 890 895

Ile Leu Asp Asp Phe Lys Val Ser Leu Glu Ser Ile Gly Ser Leu Thr
900 905 910

Gln Glu Leu Glu Tyr Arg Gly Glu Ser Leu Leu Cys Ser Leu Ile Phe
915 920 925

Arg Asn Ile Trp Leu Tyr Asn Gln Ile Ala Leu Gln Leu Arg Asn His
930 935 940

Ala Leu Cys Asn Asn Lys Leu Tyr Leu Asp Ile Leu Lys Val Leu Lys
945 950 955 960

His Leu Lys Thr Phe Phe Asn Leu Asp Ser Ile Asp Met Ala Leu Ser
965 970 975

Leu Tyr Met Asn Leu Pro Met Leu Phe Gly Gly Gly Asp Pro Asn Leu
980 985 990

Leu Tyr Arg Ser Phe Tyr Arg Arg Thr Pro Asp Phe Leu Thr Glu Ala
995 1000 1005

Ile Val His Ser Val Phe Val Leu Ser Tyr Tyr Thr Gly His Asp Leu
1010 1015 1020

Gln Asp Lys Leu Gln Asp Leu Pro Asp Asp Arg Leu Asn Lys Phe Leu
1025 1030 1035 1040

Thr Cys Val Ile Thr Phe Asp Lys Asn Pro Asn Ala Glu Phe Val Thr
1045 1050 1055

Leu Met Arg Asp Pro Gln Ala Leu Gly Ser Glu Arg Gln Ala Lys Ile
1060 1065 1070

Thr Ser Glu Ile Asn Arg Leu Ala Val Thr Glu Val Leu Ser Ile Ala
1075 1080 1085

Pro Asn Lys Ile Phe Ser Lys Ser Ala Gln His Tyr Thr Thr Thr Glu
1090 1095 1100

Ile Asp Leu Asn Asp Ile Met Gln Asn Ile Glu Pro Thr Tyr Pro His
1105 1110 1115 1120

Gly Leu Arg Val Val Tyr Glu Ser Leu Pro Phe Tyr Lys Ala Glu Lys
1125 1130 1135

Ile Val Asn Leu Ile Ser Gly Thr Lys Ser Ile Thr Asn Ile Leu Glu
1140 1145 1150

Lys Thr Ser Ala Ile Asp Thr Thr Asp Ile Asn Arg Ala Thr Asp Met
1155 1160 1165

Met Arg Lys Asn Ile Thr Leu Leu Ile Arg Ile Leu Pro Leu Asp Cys
1170 1175 1180

Asn Lys Asp Lys Arg Glu Leu Leu Ser Leu Glu Asn Leu Ser Ile Thr
1185 1190 1195 1200

Glu Leu Ser Lys Tyr Val Arg Glu Arg Ser Trp Ser Leu Ser Asn Ile
1205 1210 1215

Val Gly Val Thr Ser Pro Ser Ile Met Phe Thr Met Asp Ile Lys Tyr
1220 1225 1230

Thr Thr Ser Thr Ile Ala Ser Gly Ile Ile Ile Glu Lys Tyr Asn Val
1235 1240 1245

Asn Ser Leu Thr Arg Gly Glu Arg Gly Pro Thr Lys Pro Trp Val Gly
1250 1255 1260

Ser Ser Thr Gln Glu Lys Lys Thr Met Pro Val Tyr Asn Arg Gln Val
1265 1270 1275 1280

Leu Thr Lys Lys Gln Arg Asp Gln Ile Asp Leu Leu Ala Lys Leu Asp
1285 1290 1295

Trp Val Tyr Ala Ser Ile Asp Asn Lys Asp Glu Phe Met Glu Glu Leu
1300 1305 1310

Ser Thr Gly Thr Leu Gly Leu Ser Tyr Glu Lys Ala Lys Lys Leu Phe
1315 1320 1325

Pro Gln Tyr Leu Ser Val Asn Tyr Leu His Arg Leu Thr Val Ser Ser
1330 1335 1340

Arg Pro Cys Glu Phe Pro Ala Ser Ile Pro Ala Tyr Arg Thr Thr Asn
1345 1350 1355 1360

Tyr His Phe Asp Thr Ser Pro Ile Asn His Val Leu Thr Glu Lys Tyr
1365 1370 1375

Gly Asp Glu Asp Ile Asp Ile Val Phe Gln Asn Cys Ile Ser Phe Gly
1380 1385 1390

Leu Ser Leu Met Ser Val Val Glu Gln Phe Thr Asn Ile Cys Pro Asn
1395 1400 1405

Arg Ile Ile Leu Ile Pro Lys Leu Asn Glu Ile His Leu Met Lys Pro
    1410   1415   1420

Pro Ile Phe Thr Gly Asp Val Asp Ile Ile Lys Leu Lys Gln Val Ile
1425   1430   1435   1440

Gln Lys Gln His Met Phe Leu Pro Asp Lys Ile Ser Leu Thr Gln Tyr
                1445   1450   1455

Val Glu Leu Phe Leu Ser Asn Lys Ala Leu Lys Ser Gly Ser His Ile
            1460   1465   1470

Asn Ser Asn Leu Ile Leu Val His Lys Met Ser Asp Tyr Phe His Asn
        1475   1480   1485

Ala Tyr Ile Leu Ser Thr Asn Leu Ala Gly His Trp Ile Leu Ile Ile
    1490   1495   1500

Gln Leu Met Lys Asp Ser Lys Gly Ile Phe Glu Lys Asp Trp Gly Glu
1505   1510   1515   1520

Gly Tyr Ile Thr Asp His Met Phe Ile Asn Leu Asn Val Phe Phe Asn
                1525   1530   1535

Ala Tyr Lys Thr Tyr Leu Leu Cys Phe His Lys Gly Tyr Gly Lys Ala
            1540   1545   1550

Lys Leu Glu Cys Asp Met Asn Thr Ser Asp Leu Leu Cys Val Leu Glu
        1555   1560   1565

Leu Ile Asp Ser Ser Tyr Trp Lys Ser Met Ser Lys Val Phe Leu Glu
    1570   1575   1580

Gln Lys Val Ile Lys Tyr Ile Val Asn Gln Asp Thr Ser Leu Arg Arg
1585   1590   1595   1600

Ile Lys Gly Cys His Ser Phe Lys Leu Trp Phe Leu Lys Arg Leu Asn
                1605   1610   1615

Asn Ala Lys Phe Thr Val Cys Pro Trp Val Val Asn Ile Asp Tyr His
            1620   1625   1630

Pro Thr His Met Lys Ala Ile Leu Ser Tyr Ile Asp Leu Val Arg Met
        1635   1640   1645

Gly Leu Ile Asn Val Asp Lys Leu Thr Ile Lys Asn Lys Asn Lys Phe
    1650   1655   1660

Asn Asp Glu Phe Tyr Thr Ser Asn Leu Phe Tyr Ile Ser Tyr Asn Phe
1665   1670   1675   1680

Ser Asp Asn Thr His Leu Leu Thr Lys Gln Ile Arg Ile Ala Asn Ser

1685 1690 1695

Glu Leu Glu Asp Asn Tyr Asn Lys Leu Tyr His Pro Thr Pro Glu Thr
1700 1705 1710

Leu Glu Asn Met Ser Leu Ile Pro Val Lys Ser Asn Asn Ser Asn Lys
1715 1720 1725

Pro Lys Phe Cys Ile Ser Gly Asn Thr Glu Ser Met Met Met Ser Thr
1730 1735 1740

Phe Ser Ser Lys Met His Ile Lys Ser Ser Thr Val Thr Thr Arg Phe
1745 1750 1755 1760

Asn Tyr Ser Lys Gln Asp Leu Tyr Asn Leu Phe Pro Ile Val Val Ile
1765 1770 1775

Asp Lys Ile Ile Asp His Ser Gly Asn Thr Ala Lys Ser Asn Gln Leu
1780 1785 1790

Tyr Thr Thr Thr Ser His Gln Thr Ser Leu Val Arg Asn Ser Ala Ser
1795 1800 1805

Leu Tyr Cys Met Leu Pro Trp His His Val Asn Arg Phe Asn Phe Val
1810 1815 1820

Phe Ser Ser Thr Gly Cys Lys Ile Ser Ile Glu Tyr Ile Leu Lys Asp
1825 1830 1835 1840

Leu Lys Ile Lys Asp Pro Ser Cys Ile Ala Phe Ile Gly Glu Gly Ala
1845 1850 1855

Gly Asn Leu Leu Leu Arg Thr Val Val Glu Leu His Pro Asp Ile Arg
1860 1865 1870

Tyr Ile Tyr Arg Ser Leu Lys Asp Cys Asn Asp His Ser Leu Pro Ile
1875 1880 1885

Glu Phe Leu Arg Leu Tyr Asn Gly His Ile Asn Ile Asp Tyr Gly Glu
1890 1895 1900

Asn Leu Thr Ile Pro Ala Thr Asp Ala Thr Asn Asn Ile His Trp Ser
1905 1910 1915 1920

Tyr Leu His Ile Lys Phe Ala Glu Pro Ile Ser Ile Phe Val Cys Asp
1925 1930 1935

Ala Glu Leu Pro Val Thr Ala Asn Trp Ser Lys Ile Ile Ile Glu Trp
1940 1945 1950

Ser Lys His Val Arg Lys Cys Lys Tyr Cys Ser Ser Val Asn Arg Cys
1955 1960 1965

Ile Leu Ile Ala Lys Tyr His Ala Gln Asp Asp Ile Asp Phe Lys Leu
1970 1975 1980

Asp Asn Ile Thr Ile Leu Lys Thr Tyr Val Cys Leu Gly Ser Lys Leu
1985 1990 1995 2000

Lys Gly Ser Glu Val Tyr Leu Ile Leu Thr Ile Gly Pro Ala Asn Ile
2005 2010 2015

Leu Pro Val Phe Asp Val Val Gln Asn Ala Lys Leu Ile Leu Ser Arg
2020 2025 2030

Thr Lys Asn Phe Ile Met Pro Lys Lys Thr Asp Lys Glu Ser Ile Asp
2035 2040 2045

Ala Asp Ile Lys Ser Leu Ile Pro Phe Leu Cys Tyr Pro Ile Thr Lys
2050 2055 2060

Lys Gly Ile Lys Thr Ser Leu Ser Lys Leu Lys Ser Val Val Asn Gly
2065 2070 2075 2080

Asp Ile Leu Ser Tyr Ser Ile Ala Gly Arg Asn Glu Val Phe Ser Asn
2085 2090 2095

Lys Leu Ile Asn His Lys His Met Asn Ile Leu Lys Trp Leu Asp His
2100 2105 2110

Val Leu Asn Phe Arg Ser Ala Glu Leu Asn Tyr Asn His Leu Tyr Met
2115 2120 2125

Ile Glu Ser Thr Tyr Pro Tyr Leu Ser Glu Leu Leu Asn Ser Leu Thr
2130 2135 2140

Thr Asn Glu Leu Lys Lys Leu Ile Lys Ile Thr Gly Ser Val Leu Tyr
2145 2150 2155 2160

Asn Leu Pro Asn Glu Gln
2165

(2) INFORMATION FOR SEQ ID NO:31:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 15219 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:31:

ACGGGAAAAA AATGCGTACT ACAAACTTGC ACATTCGAAA AAAATGGGGC AAATAAGAAC 60

TTGATAAGTG CTATTTAAGT CTAACCTTTT CAATCAGAAA TGGGGTGCAA TTCACTGAGC 120

ATGATAAAGG TTAGATTACA AAATTTATTT GACAATGACG AAGTAGCATT GTTAAAAATA 180

ACATGTTATA CTGATAAATT AATTCTTCTG ACCAATGCAT TAGCCAAAGC AGCAATACAT 240

ACAATTAAAT TAAACGGCAT AGTTTTTATA CATGTTATAA CAAGCAGTGA AGTGTGCCCT 300

GATAACAATA TTGTAGTGAA ATCTAACTTT ACAACAATGC CAATACTACA AAATGGAGGA 360

TACATATGGG AATTGATTGA GTTGACACAC TGCTCTCAAT TAAACGGTTT AATGGATGAT 420

AATTGTGAAA TCAAATTTTC TAAAAGACTA AGTGACTCAG TAATGACTAA TTATATGAAT 480

CAAATATCTG ACTTACTTGG GCTTGATCTC AATTCATGAA TTATGTTTAG TCTAATTCAA 540

TAGACATGTG TTTATTACCA TTTTAGTTAA TATAAAAACT CATCAAAGGG AAATGGGGCA 600

AATAAACTCA CCTAATCAAT CAAACCATGA GCACTACAAA TGACAACACT ACTATGCAAA 660

GATTGATGAT CACAGACATG AGACCCCTGT CAATGGATTC AATAATAACA TCTCTTACCA 720

AAGAAATCAT CACACACAAA TTCATATACT TGATAAACAA TGAATGTATT GTAAGAAAAC 780

TTGATGAAAG ACAAGCTACA TTTACATTCT TAGTCAATTA TGAGATGAAG CTACTGCACA 840

AAGTAGGGAG TACCAAATAC AAAAAATACA CTGAATATAA TACAAAATAT GGCACTTTCC 900

CCATGCCTAT ATTTATCAAT CACGGCGGGT TTCTAGAATG TATTGGCATT AAGCCTACAA 960

AACACACTCC TATAATATAC AAATATGACC TCAACCCGTG AATTCCAACA AAAAAACCAA 1020

CCCAACCAAA CCAAACTATT CCTCAAACAA CAGTGCTCAA TAGTTAAGAA GGAGCTAATC 1080

CATTTTAGTA ATTAAAAATA AAAGTAAAGC CAATAACATA AATTGGGGCA AATACAAAGA 1140

TGGCTCTTAG CAAAGTCAAG TTGAATGATA CATTAAATAA GGATCAGCTG CTGTCATCCA 1200

GCAAATACAC TATTCAACGT AGTACAGGAG ATAATATTGA CACTCCCAAT TATGATGTGC 1260

AAAAACACCT AAACAAACTA TGTGGTATGC TATTAATCAC TGAAGATGCA AATCATAAAT 1320

TCACAGGATT AATAGGTATG TTATATGCTA TGTCCAGGTT AGGAAGGGAA GACACTATAA 1380

AGATACTTAA AGATGCTGGA TATCATGTTA AAGCTAATGG AGTAGATATA ACAACATATC 1440

GTCAAGATAT AAATGGAAAG GAAATGAAAT TCGAAGTATT AACATTATCA AGCTTGACAT 1500

CAGAAATACA AGTCAATATT GAGATAGAAT CTAGAAAGTC CTACAAAAAA ATGCTAAAAG 1560

AGATGGGAGA AGTGGCTCCA GAATATAGGC ATGATTCTCC AGACTGTGGG ATGATAATAC 1620

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CAGTAATTAG GAGGGCAAAC AATGTCTTAA AAAACGAAAT AAAACGATAC AAGGGCCTCA 1740

TACCAAAGGA TATAGCTAAC AGTTTTTATG AAGTGTTTGA AAAACACCCT CATCTTATAG 1800

ATGTTTTCGT GCACTTTGGC ATTGCACAAT CATCCACAAG AGGGGGTAGT AGAGTTGAAG 1860

GAATCTTTGC AGGATTGTTT ATGAATGCCT ATGGTTCAGG GCAAGTAATG CTAAGATGGG 1920

GAGTTTTAGC CAAATCTGTA AAAAATATCA TGCTAGGACA TGCTAGTGTC CAGGCAGAAA 1980

TGGAGCAAGT TGTGGAAGTC TATGAGTATG CACAGAAGTT GGGAGGAGAA GCTGGATTCT 2040

ACCATATATT GAACAATCCA AAAGCATCAT TGCTGTCATT AACTCAATTT CCCAACTTCT 2100

CAAGTGTGGT CCTAGGCAAT GCAGCAGGTC TAGGCATAAT GGGAGAGTAT AGAGGTACAC 2160

CAAGAAACCA GGATCTTTAT GATGCAGCTA AAGCATATGC AGAGCAACTC AAAGAAAATG 2220

GAGTAATAAA CTACAGTGTA TTAGACTTAA CAGCAGAAGA ATTGGAAGCC ATAAAGCATC 2280

AACTCAACCC CAAAGAAGAT GATGTAGAGC TTTAAGTTAA CAAAAAATAC GGGGCAAATA 2340

AGTCAACATG GAGAAGTTTG CACCTGAATT TCATGGAGAA GATGCAAATA ACAAAGCTAC 2400

CAAATTCCTA GAATCAATAA AGGGCAAGTT CGCATCATCC AAAGATCCTA AGAAGAAAGA 2460

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TAGGAATGAG GAAAGCGAAA AAATGGCAAA AGACACCTCA GATGAAGTGT CTCTTAATCC 3000

AACTTCCAAA AAATTGAGTG ACTTGTTGGA AGACAACGAT AGTGACAATG ATCTATCACT 3060

TGATGATTTT TGATCAGCGA TCAACTCACT CAGCAATCAA CAACATCAAT AAAACAGACA 3120

TCAATCCATT GAATCAACTG CCAGACCGAA CAAACAAACG TCCATCAGTA GAACCACCAA 3180

CCAATCAATC AACCAATTGA TCAATCAGCA ACCCGACAAA ATTAACAATA TAGTAACAAA 3240

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AATATGGGTG CCTATGTTCC AGTCATCTGT GCCAGCAGAC TTGCTCATAA AAGAACTTGC 3420

AAGCATCAAT ATACTAGTGA AGCAGATCTC TACGCCCAAA GGACCTTCAC TACGAGTCAC 3480

GATTAACTCA AGAAGTGCTG TGCTGGCTCA AATGCCTAGT AATTTCATCA TAAGCGCAAA 3540

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AGCATGCAGT CTAACATGCT TAAAAGTAAA AAGTATGTTA ACTACAGTCA AAGATCTTAC 3660

CATGAAGACA TTCAACCCCA CTCATGAGAT CATTGCTCTA TGTGAATTTG AAAATATTAT 3720

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TCTGAACTCA CTAGAAAATA TAGCAACCAC CGAATTCAAA AATGCTATCA CCAATGCAAA 3840

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ACAATAGAAC TCACAAGCAA ATTTTGGCCC TATTTTACAC TAATACATAT GATCTTAACT 4380

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AGTTCCACCA TTATGCTGTG TCAAACCATA ATCCTGTATA TACAAACAAA CAAATCCAAT 4560

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ACAGTCCAAC AGCAATCCCT CCTCTCAACC ACCCCCGAAA ACACACCCAA CTCCACACAA 5520

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ATTACCAAGT GAAGTCAGCC TTTGTAACAC TGACATATTC AATTCCAAGT ATGACTGCAA 6840

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CACTTTATAC TATGTAAACA AGCTGGAAGG CAAGAACCTT TATGTAAAAG GGGAACCTAT 7080

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AGTCAATGAA AAAATCAATC AAAGTTTAGC TTTTATTCGT AGATCTGATG AATTACTACA 7200

TAATGTAAAT ACTGGCAAAT CTACTACAAA TATTATGATA ACTACAATTA TTATAGTAAT 7260

CATTGTAGTA TTGTTATCAT TAATAGCTAT TGGTTTACTG TTGTATTGTA AAGCCAAAAA 7320

CACACCAGTT ACACTAAGCA AAGACCAACT AAGTGGAATC AATAATATTG CATTCAGCAA 7380

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AACAAGATAC TCAAGTCAAT GGACAAAAGC ATAGACACTT TGTCTGAAAT AAGTGGAGCT 7800

GCTGAACTGG ATAGAACAGA AGAATATGCT CTTGGTATAG TTGGAGTGCT AGAGAGTTAC 7860

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CATATTGATC TCAAGTGAAA GCATGGTTGC TACATTCAAT CATAAAAACA TATTACAATT 8280

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TGAAGATATA TATACAGTAT ATATATTAGT GTCATAATGC TTGACCATAA CGACTCTATG 8460

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ACAACACTCT TGAAAAAATT GATGTGTTCA ATGCAACATC CTCCATCATG GTTAATACAC 9120

TGGTTCAATT TATATACAAA ATTAAATAAC ATATTAACAC AATATCGATC AAATGAGGTA 9180

AAAAGTCATG GGTTTATATT AATAGATAAT CAAACTTTAA GTGGTTTTCA GTTTATTTTA 9240

AATCAATATG GTTGTATCGT TTATCATAAA GGACTCAAAA AAATCACAAC TACTACTTAC 9300

AATCAATTTT TGACATGGAA AGACATCAGC CTTAGCAGAT TAAATGTTTG CTTAATTACT 9360

TGGATAAGTA ATTGTTTAAA TACATTAAAC AAAAGCTTAG GGCTGAGATG TGGATTCAAT 9420

AATGTTGTGT TATCACAATT ATTTCTTTAT GGAGATTGTA TACTGAAATT ATTTCATAAT 9480

GAAGGCTTCT ACATAATAAA AGAAGTAGAG GGATTTATTA TGTCTTTAAT TCTAAACATA 9540

ACAGAAGAAG ATCAATTTAA GAAACGATTT TATAATAGCA TGCTAAATAA CATCACAGAT 9600

GCAGCTATTA AGGCTCAAAA GGACCTACTA TCAAGAGTAT GTCACACTTT ATTAGACAAG 9660

ACAGTGTCTG ATAATATCAT AAATGGTAAA TGGATAATCC TATTAAGTAA ATTTCTTAAA 9720

TTGATTAAGC TTGCAGGTGA TAATAATCTC AATAACTTGA GTGAGCTATA TTTTCTCTTC 9780

AGAATCTTTG GACATCCAAT GGTCGATGAA AGACAAGCAA TGGATTCTGT AAGAATTAAC 9840

TGTAATGAAA CTAAGTTCTA CTTATTAAGT AGTCTAAGTA CATTAAGAGG TGCTTTCATT 9900

TATAGAATCA TAAAAGGGTT TGTAAATACC TACAACAGAT GGCCCACCTT AAGGAATGCT 9960

ATTGTCCTAC CTCTAAGATG GTTAAACTAC TATAAACTTA ATACTTATCC ATCTCTACTT 10020

GAAATCACAG AAAATGATTT GATTATTTTA TCAGGATTGC GGTTCTATCG TGAGTTTCAT 10080

CTGCCTAAAA AAGTGGATCT TGAAATGATA ATAAATGACA AAGCCATTTC ACCTCCAAAA 10140

GATCTAATAT GGACTAGTTT TCCTAGAAAT TACATGCCAT CACATATACA AAATTATATA 10200

GAACATGAAA AGTTGAAGTT CTCTGAAAGC GACAGATCGA GAAGAGTACT AGAGTATTAC 10260

TTGAGAGATA ATAAATTCAA TGAATGCGAT CTATACAATT GTGTAGTCAA TCAAAGCTAT 10320

CTCAACAACT CTAATCACGT GGTATCACTA ACTGGTAAAG AAAGAGAGCT CAGTGTAGGT 10380

AGAATGTTTG CTATGCAACC AGGTATGTTT AGGCAAATCC AAATCTTAGC AGAGAAAATG 10440

ATAGCTGAAA ATATTTTACA ATTCTTCCCT GAGAGTTTGA CAAGATATGG TGATCTAGAG 10500

CTTCAAAAGA TATTAGAATT AAAAGCAGGA ATAAGCAACA AGTCAAATCG TTATAATGAT 10560

AACTACAACA ATTATATCAG TAAATGTTCT ATCATTACAG ATCTTAGCAA ATTCAATCAG 10620

GCATTTAGAT ATGAAACATC ATGTATCTGC AGTGATGTAT TAGATGAACT GCATGGAGTA 10680

CAATCTCTGT TCTCTTGGTT GCATTTAACA ATACCTCTTG TCACAATAAT ATGTACATAT 10740

AGACATGCAC CTCCTTTCAT AAAGGATCAT GTTGTTAATC TTAATGAGGT TGATGAACAA 10800

AGTGGATTAT ACAGATATCA TATGGGTGGT ATTGAGGGCT GGTGTCAAAA ACTGTGGACC 10860

ATTGAAGCTA TATCATTATT AGATCTAATA TCTCTCAAAG GGAAATTCTC TATCACAGCT 10920

CTGATAAATG GTGATAATCA GTCAATTGAT ATAAGCAAAC CAGTTAGACT TATAGAGGGT 10980

CAGACCCATG CACAAGCAGA TTATTTGTTA GCATTAAATA GCCTTAAATT GTTATATAAA 11040

GAGTATGCAG GTATAGGCCA TAAGCTTAAG GGAACAGAGA CCTATATATC CCGAGATATG 11100

CAGTTCATGA GCAAAACAAT CCAGCACAAT GGAGTGTACT ATCCAGCCAG TATCAAAAAA 11160

GTCCTGAGAG TAGGTCCATG GATAAACACG ATACTTGATG ATTTTAAAGT TAGTTTAGAA 11220

TCTATAGGCA GCTTAACACA GGAGTTAGAA TACAGAGGAG AAAGCTTATT ATGCAGTTTA 11280

ATATTTAGGA ACATTTGGTT ATACAATCAA ATTGCTTTGC AACTCCGAAA TCATGCATTA 11340

TGTAACAATA AGCTATATTT AGATATATTG AAAGTATTAA AACACTTAAA AACTTTTTTT 11400

AATCTTGATA GCATTGATAT GGCTTTATCA TTGTATATGA ATTTGCCTAT GCTGTTTGGT 11460

GGTGGTGATC CTAATTTGTT ATATCGAAGC TTTTATAGGA GAACTCCAGA CTTCCTTACA 11520

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AAGCTCCAGG ATCTTCCAGA TGATAGACTG AACAAATTCT TGACATGTGT CATCACATTT 11640

GATAAAAATC CCAATGCCGA GTTTGTAACA TTGATGAGGG ATCCACAGGC TTTAGGGTCT 11700

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ATAGCCCCAA ACAAAATATT TTCTAAAAGT GCACAACATT ATACTACCAC TGAGATTGAT 11820

CTAAATGACA TTATGCAAAA TATAGAACCA ACTTACCCTC ATGGATTAAG AGTTGTTTAT 11880

GAAAGTTTAC CTTTTTATAA AGCAGAAAAA ATAGTTAATC TTATATCAGG AACAAAATCC 11940

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AGAGAAAGAT CTTGGTCATT ATCCAATATA GTAGGAGTAA CATCGCCAAG TATTATGTTC 12180

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AATGTTAATA GTTTAACTCG TGGTGAAAGA GGACCCACCA AGCCATGGGT AGGCTCATCC 12300

ACGCAGGAGA AAAAAACAAT GCCAGTGTAC AACAGACAAG TTTTAACCAA AAAGCAAAGA 12360

GACCAAATAG ATTTATTAGC AAAATTAGAC TGGGTATATG CATCCATAGA CAACAAAGAT 12420

GAATTCATGG AAGAACTGAG TACTGGAACA CTTGGACTGT CATATGAAAA AGCCAAAAAG 12480
TTGTTTCCAC AATATCTAAG TGTCAATTAT TTACACCGTT TAACAGTCAG TAGTAGACCA 12540
TGTGAATTCC CTGCATCAAT ACCAGCTTAT AGAACAACAA ATTATCATTT TGATACTAGT 12600
CCTATCAATC ATGTATTAAC AGAAAAGTAT GGAGATGAAG ATATCGACAT TGTGTTTCAA 12660
AATTGCATAA GTTTTGGTCT TAGCCTGATG TCGGTTGTGG AACAATTCAC AAACATATGT 12720
CCTAATAGAA TTATTCTCAT ACCGAAGCTG AATGAGATAC ATTTGATGAA ACCTCCTATA 12780
TTTACAGGAG ATGTTGATAT CATCAAGTTG AAGCAAGTGA TACAAAAGCA GCACATGTTC 12840
CTACCAGATA AAATAAGTTT AACCCAATAT GTAGAATTAT TCTTAAGTAA CAAAGCACTT 12900
AAATCTGGAT CTCACATCAA CTCTAATTTA ATATTAGTAC ATAAAATGTC TGATTATTTT 12960
CATAATGCTT ATATTTTAAG TACTAATTTA GCTGGACATT GGATTCTGAT TATTCAACTT 13020
ATGAAAGATT CAAAAGGTAT TTTTGAAAAA GATTGGGGAG AGGGGTACAT AACTGATCAT 13080
ATGTTCATTA ATTTGAATGT TTTCTTTAAT GCTTATAAGA CTTATTTGCT ATGTTTTCAT 13140
AAAGGTTATG GTAAAGCAAA ATTAGAATGT GATATGAACA CTTCAGATCT TCTTTGTGTT 13200
TTGGAGTTAA TAGACAGTAG CTACTGGAAA TCTATGTCTA AAGTTTTCCT AGAACAAAAA 13260
GTCATAAAAT ACATAGTCAA TCAAGACACA AGTTTGCGTA GAATAAAAGG CTGTCACAGT 13320
TTTAAGTTGT GGTTTTTAAA ACGCCTTAAT AATGCTAAAT TTACCGTATG CCCTTGGGTT 13380
GTTAACATAG ATTATCACCC AACACACATG AAAGCTATAT TATCTTACAT AGATTTAGTT 13440
AGAATGGGGT TAATAAATGT AGATAAATTA ACCATTAAAA ATAAAAACAA ATTCAATGAT 13500
GAATTTTACA CATCAAATCT CTTTTACATT AGTTATAACT TTTCAGACAA CACTCATTTG 13560
CTAACAAAAC AAATAAGAAT TGCTAATTCA GAATTAGAAG ATAATTATAA CAAACTATAT 13620
CACCCAACCC CAGAAACTTT AGAAAATATG TCATTAATTC CTGTTAAAAG TAATAATAGT 13680
AACAAACCTA AATTTTGTAT AAGTGGAAAT ACCGAATCTA TGATGATGTC AACATTCTCT 13740
AGTAAAATGC ATATTAAATC TTCCACTGTT ACCACAAGAT TCAATTATAG CAAACAAGAC 13800
TTGTACAATT TATTTCCAAT TGTTGTGATA GACAAGATTA TAGATCATTC AGGTAATACA 13860
GCAAAATCTA ACCAACTTTA CACCACCACT TCACATCAGA CATCTTTAGT AAGGAATAGT 13920
GCATCACTTT ATTGCATGCT TCCTTGGCAT CATGTCAATA GATTTAACTT TGTATTTAGT 13980

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TCCACAGGAT GCAAGATCAG TATAGAGTAT ATTTTAAAAG ATCTTAAGAT TAAGGACCCC   14040
AGTTGTATAG CATTCATAGG TGAAGGAGCT GGTAACTTAT TATTACGTAC GGTAGTAGAA   14100
CTTCATCCAG ACATAAGATA CATTTACAGA AGTTTAAAAG ATTGCAATGA TCATAGTTTA   14160
CCTATTGAAT TTCTAAGGTT ATACAACGGG CATATAAACA TAGATTATGG TGAGAATTTA   14220
ACCATTCCTG CTACAGATGC AACTAATAAC ATTCATTGGT CTTATTTACA TATAAAATTT   14280
GCAGAACCTA TTAGCATCTT TGTCTGCGAT GCTGAATTAC CTGTTACAGC CAATTGGAGT   14340
AAAATTATAA TTGAATGGAG TAAGCATGTA AGAAAGTGCA AGTACTGTTC TTCTGTAAAT   14400
AGATGCATTT TAATTGCAAA ATATCATGCT CAAGATGACA TTGATTTCAA ATTAGATAAC   14460
ATTACTATAT TAAAAACTTA CGTGTGCCTA GGTAGCAAGT TAAAAGGATC TGAAGTTTAC   14520
TTAATCCTTA CAATAGGCCC TGCAAATATA CTTCCTGTTT TTGATGTTGT ACAAAATGCT   14580
AAATTGATAC TTTCAAGAAC TAAAAATTTC ATTATGCCTA AAAAAACTGA CAAGGAATCT   14640
ATCGATGCAA ATATTAAAAG CTTAATACCT TTCCTTTGTT ACCCTATAAC AAAAAAAGGA   14700
ATTAAGACTT CATTGTCAAA ATTGAAGAGT GTAGTTAATG GAGATATATT ATCATATTCT   14760
ATAGCTGGAC GTAATGAAGT ATTCAGCAAC AAGCTTATAA ACCACAAGCA TATGAATATC   14820
CTAAAATGGC TAGATCATGT TTTAAATTTT AGATCAGCTG AACTTAATTA CAATCATTTA   14880
TACATGATAG AGTCCACATA TCCTTACTTA AGTGAATTGT TAAATAGTTT AACAACCAAT   14940
GAGCTCAAGA AGCTGATTAA AATAACAGGT AGTGTGCTAT ACAACCTTCC CAACGAACAG   15000
TAGTTTAAAA TATCATTAAC AAGTTTGGTC AAATTTAGAT GCTAACACAT CATTATATTA   15060
TAGTTATTAA AGAATATACA AACTTTTCAA TAATTTAGCA TATTGATTCC AAAATTATCA   15120
TTTTAGTCTT AAGGGGTTAA ATAAAAGTCT AAAACTAACA ATTATACATG TGCATTCACA   15180
ACACAACGAG ACATTAGTTT TTGACACTTT TTTTCTCGT                          15219
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(2) INFORMATION FOR SEQ ID NO:32:

(i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 2166 amino acids
- (B) TYPE: amino acid
- (C) STRANDEDNESS:
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:32:

Met Asp Pro Ile Ile Asn Gly Asn Ser Ala Asn Val Tyr Leu Thr Asp
1 5 10 15

Ser Tyr Leu Lys Gly Val Ile Ser Phe Ser Glu Cys Asn Ala Leu Gly
20 25 30

Ser Tyr Leu Phe Asn Gly Pro Tyr Leu Lys Asn Asp Tyr Thr Asn Leu
35 40 45

Ile Ser Arg Gln Ser Pro Leu Leu Glu His Met Asn Leu Lys Lys Leu
50 55 60

Thr Ile Thr Gln Ser Leu Ile Ser Arg Tyr His Lys Gly Glu Leu Lys
65 70 75 80

Leu Glu Glu Pro Thr Tyr Phe Gln Ser Leu Leu Met Thr Tyr Lys Ser
85 90 95

Met Ser Ser Ser Glu Gln Ile Ala Thr Thr Asn Leu Leu Lys Lys Ile
100 105 110

Ile Arg Arg Ala Ile Glu Ile Ser Asp Val Lys Val Tyr Ala Ile Leu
115 120 125

Asn Lys Leu Gly Leu Lys Glu Lys Asp Arg Val Lys Pro Asn Asn Asn
130 135 140

Ser Gly Asp Glu Asn Ser Val Leu Thr Thr Ile Ile Lys Asp Asp Ile
145 150 155 160

Leu Ser Ala Val Glu Asn Asn Gln Ser Tyr Thr Asn Ser Asp Lys Ser
165 170 175

His Ser Val Asn Gln Asn Ile Thr Ile Lys Thr Thr Leu Leu Lys Lys
180 185 190

Leu Met Cys Ser Met Gln His Pro Pro Ser Trp Leu Ile His Trp Phe
195 200 205

Asn Leu Tyr Thr Lys Leu Asn Asn Ile Leu Thr Gln Tyr Arg Ser Asn
210 215 220

Glu Val Lys Ser His Gly Phe Ile Leu Ile Asp Asn Gln Thr Leu Ser
225 230 235 240

Gly Phe Gln Phe Ile Leu Asn Gln Tyr Gly Cys Ile Val Tyr His Lys

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                245                 250                 255

Gly Leu Lys Lys Ile Thr Thr Thr Thr Tyr Asn Gln Phe Leu Thr Trp
            260                 265                 270

Lys Asp Ile Ser Leu Ser Arg Leu Asn Val Cys Leu Ile Thr Trp Ile
        275                 280                 285

Ser Asn Cys Leu Asn Thr Leu Asn Lys Ser Leu Gly Leu Arg Cys Gly
    290                 295                 300

Phe Asn Asn Val Val Leu Ser Gln Leu Phe Leu Tyr Gly Asp Cys Ile
305                 310                 315                 320

Leu Lys Leu Phe His Asn Glu Gly Phe Tyr Ile Ile Lys Glu Val Glu
                325                 330                 335

Gly Phe Ile Met Ser Leu Ile Leu Asn Ile Thr Glu Glu Asp Gln Phe
            340                 345                 350

Lys Lys Arg Phe Tyr Asn Ser Met Leu Asn Asn Ile Thr Asp Ala Ala
        355                 360                 365

Ile Lys Ala Gln Lys Asp Leu Leu Ser Arg Val Cys His Thr Leu Leu
    370                 375                 380

Asp Lys Thr Val Ser Asp Asn Ile Ile Asn Gly Lys Trp Ile Ile Leu
385                 390                 395                 400

Leu Ser Lys Phe Leu Lys Leu Ile Lys Leu Ala Gly Asp Asn Asn Leu
                405                 410                 415

Asn Asn Leu Ser Glu Leu Tyr Phe Leu Phe Arg Ile Phe Gly His Pro
            420                 425                 430

Met Val Asp Glu Arg Gln Ala Met Asp Ser Val Arg Ile Asn Cys Asn
        435                 440                 445

Glu Thr Lys Phe Tyr Leu Leu Ser Ser Leu Ser Thr Leu Arg Gly Ala
    450                 455                 460

Phe Ile Tyr Arg Ile Ile Lys Gly Phe Val Asn Thr Tyr Asn Arg Trp
465                 470                 475                 480

Pro Thr Leu Arg Asn Ala Ile Val Leu Pro Leu Arg Trp Leu Asn Tyr
                485                 490                 495

Tyr Lys Leu Asn Thr Tyr Pro Ser Leu Leu Glu Ile Thr Glu Asn Asp
            500                 505                 510

Leu Ile Ile Leu Ser Gly Leu Arg Phe Tyr Arg Glu Phe His Leu Pro
        515                 520                 525
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Lys Lys Val Asp Leu Glu Met Ile Ile Asn Asp Lys Ala Ile Ser Pro
530 535 540

Pro Lys Asp Leu Ile Trp Thr Ser Phe Pro Arg Asn Tyr Met Pro Ser
545 550 555 560

His Ile Gln Asn Tyr Ile Glu His Glu Lys Leu Lys Phe Ser Glu Ser
565 570 575

Asp Arg Ser Arg Arg Val Leu Glu Tyr Tyr Leu Arg Asp Asn Lys Phe
580 585 590

Asn Glu Cys Asp Leu Tyr Asn Cys Val Val Asn Gln Ser Tyr Leu Asn
595 600 605

Asn Ser Asn His Val Val Ser Leu Thr Gly Lys Glu Arg Glu Leu Ser
610 615 620

Val Gly Arg Met Phe Ala Met Gln Pro Gly Met Phe Arg Gln Ile Gln
625 630 635 640

Ile Leu Ala Glu Lys Met Ile Ala Glu Asn Ile Leu Gln Phe Phe Pro
645 650 655

Glu Ser Leu Thr Arg Tyr Gly Asp Leu Glu Leu Gln Lys Ile Leu Glu
660 665 670

Leu Lys Ala Gly Ile Ser Asn Lys Ser Asn Arg Tyr Asn Asp Asn Tyr
675 680 685

Asn Asn Tyr Ile Ser Lys Cys Ser Ile Ile Thr Asp Leu Ser Lys Phe
690 695 700

Asn Gln Ala Phe Arg Tyr Glu Thr Ser Cys Ile Cys Ser Asp Val Leu
705 710 715 720

Asp Glu Leu His Gly Val Gln Ser Leu Phe Ser Trp Leu His Leu Thr
725 730 735

Ile Pro Leu Val Thr Ile Ile Cys Thr Tyr Arg His Ala Pro Pro Phe
740 745 750

Ile Lys Asp His Val Val Asn Leu Asn Glu Val Asp Glu Gln Ser Gly
755 760 765

Leu Tyr Arg Tyr His Met Gly Gly Ile Glu Gly Trp Cys Gln Lys Leu
770 775 780

Trp Thr Ile Glu Ala Ile Ser Leu Leu Asp Leu Ile Ser Leu Lys Gly
785 790 795 800

Lys Phe Ser Ile Thr Ala Leu Ile Asn Gly Asp Asn Gln Ser Ile Asp
805 810 815

Ile Ser Lys Pro Val Arg Leu Ile Glu Gly Gln Thr His Ala Gln Ala
820 825 830

Asp Tyr Leu Leu Ala Leu Asn Ser Leu Lys Leu Leu Tyr Lys Glu Tyr
835 840 845

Ala Gly Ile Gly His Lys Leu Lys Gly Thr Glu Thr Tyr Ile Ser Arg
850 855 860

Asp Met Gln Phe Met Ser Lys Thr Ile Gln His Asn Gly Val Tyr Tyr
865 870 875 880

Pro Ala Ser Ile Lys Lys Val Leu Arg Val Gly Pro Trp Ile Asn Thr
885 890 895

Ile Leu Asp Asp Phe Lys Val Ser Leu Glu Ser Ile Gly Ser Leu Thr
900 905 910

Gln Glu Leu Glu Tyr Arg Gly Glu Ser Leu Leu Cys Ser Leu Ile Phe
915 920 925

Arg Asn Ile Trp Leu Tyr Asn Gln Ile Ala Leu Gln Leu Arg Asn His
930 935 940

Ala Leu Cys Asn Asn Lys Leu Tyr Leu Asp Ile Leu Lys Val Leu Lys
945 950 955 960

His Leu Lys Thr Phe Phe Asn Leu Asp Ser Ile Asp Met Ala Leu Ser
965 970 975

Leu Tyr Met Asn Leu Pro Met Leu Phe Gly Gly Gly Asp Pro Asn Leu
980 985 990

Leu Tyr Arg Ser Phe Tyr Arg Arg Thr Pro Asp Phe Leu Thr Glu Ala
995 1000 1005

Ile Val His Ser Val Phe Val Leu Ser Tyr Tyr Thr Gly His Asp Leu
1010 1015 1020

Gln Asp Lys Leu Gln Asp Leu Pro Asp Asp Arg Leu Asn Lys Phe Leu
1025 1030 1035 1040

Thr Cys Val Ile Thr Phe Asp Lys Asn Pro Asn Ala Glu Phe Val Thr
1045 1050 1055

Leu Met Arg Asp Pro Gln Ala Leu Gly Ser Glu Arg Gln Ala Lys Ile
1060 1065 1070

Thr Ser Glu Ile Asn Arg Leu Ala Val Thr Glu Val Leu Ser Ile Ala

1075 1080 1085

Pro Asn Lys Ile Phe Ser Lys Ser Ala Gln His Tyr Thr Thr Thr Glu
1090 1095 1100

Ile Asp Leu Asn Asp Ile Met Gln Asn Ile Glu Pro Thr Tyr Pro His
1105 1110 1115 1120

Gly Leu Arg Val Val Tyr Glu Ser Leu Pro Phe Tyr Lys Ala Glu Lys
1125 1130 1135

Ile Val Asn Leu Ile Ser Gly Thr Lys Ser Ile Thr Asn Ile Leu Glu
1140 1145 1150

Lys Thr Ser Ala Ile Asp Thr Thr Asp Ile Asn Arg Ala Thr Asp Met
1155 1160 1165

Met Arg Lys Asn Ile Thr Leu Leu Ile Arg Ile Leu Pro Leu Asp Cys
1170 1175 1180

Asn Lys Asp Lys Arg Glu Leu Leu Ser Leu Glu Asn Leu Ser Ile Thr
1185 1190 1195 1200

Glu Leu Ser Lys Tyr Val Arg Glu Arg Ser Trp Ser Leu Ser Asn Ile
1205 1210 1215

Val Gly Val Thr Ser Pro Ser Ile Met Phe Thr Met Asn Ile Lys Tyr
1220 1225 1230

Thr Thr Ser Thr Ile Ala Ser Gly Ile Ile Ile Glu Lys Tyr Asn Val
1235 1240 1245

Asn Ser Leu Thr Arg Gly Glu Arg Gly Pro Thr Lys Pro Trp Val Gly
1250 1255 1260

Ser Ser Thr Gln Glu Lys Lys Thr Met Pro Val Tyr Asn Arg Gln Val
1265 1270 1275 1280

Leu Thr Lys Lys Gln Arg Asp Gln Ile Asp Leu Leu Ala Lys Leu Asp
1285 1290 1295

Trp Val Tyr Ala Ser Ile Asp Asn Lys Asp Glu Phe Met Glu Glu Leu
1300 1305 1310

Ser Thr Gly Thr Leu Gly Leu Ser Tyr Glu Lys Ala Lys Lys Leu Phe
1315 1320 1325

Pro Gln Tyr Leu Ser Val Asn Tyr Leu His Arg Leu Thr Val Ser Ser
1330 1335 1340

Arg Pro Cys Glu Phe Pro Ala Ser Ile Pro Ala Tyr Arg Thr Thr Asn
1345 1350 1355 1360

Tyr His Phe Asp Thr Ser Pro Ile Asn His Val Leu Thr Glu Lys Tyr
1365 1370 1375

Gly Asp Glu Asp Ile Asp Ile Val Phe Gln Asn Cys Ile Ser Phe Gly
1380 1385 1390

Leu Ser Leu Met Ser Val Val Glu Gln Phe Thr Asn Ile Cys Pro Asn
1395 1400 1405

Arg Ile Ile Leu Ile Pro Lys Leu Asn Glu Ile His Leu Met Lys Pro
1410 1415 1420

Pro Ile Phe Thr Gly Asp Val Asp Ile Ile Lys Leu Lys Gln Val Ile
1425 1430 1435 1440

Gln Lys Gln His Met Phe Leu Pro Asp Lys Ile Ser Leu Thr Gln Tyr
1445 1450 1455

Val Glu Leu Phe Leu Ser Asn Lys Ala Leu Lys Ser Gly Ser His Ile
1460 1465 1470

Asn Ser Asn Leu Ile Leu Val His Lys Met Ser Asp Tyr Phe His Asn
1475 1480 1485

Ala Tyr Ile Leu Ser Thr Asn Leu Ala Gly His Trp Ile Leu Ile Ile
1490 1495 1500

Gln Leu Met Lys Asp Ser Lys Gly Ile Phe Glu Lys Asp Trp Gly Glu
1505 1510 1515 1520

Gly Tyr Ile Thr Asp His Met Phe Ile Asn Leu Asn Val Phe Phe Asn
1525 1530 1535

Ala Tyr Lys Thr Tyr Leu Leu Cys Phe His Lys Gly Tyr Gly Lys Ala
1540 1545 1550

Lys Leu Glu Cys Asp Met Asn Thr Ser Asp Leu Leu Cys Val Leu Glu
1555 1560 1565

Leu Ile Asp Ser Ser Tyr Trp Lys Ser Met Ser Lys Val Phe Leu Glu
1570 1575 1580

Gln Lys Val Ile Lys Tyr Ile Val Asn Gln Asp Thr Ser Leu Arg Arg
1585 1590 1595 1600

Ile Lys Gly Cys His Ser Phe Lys Leu Trp Phe Leu Lys Arg Leu Asn
1605 1610 1615

Asn Ala Lys Phe Thr Val Cys Pro Trp Val Val Asn Ile Asp Tyr His
1620 1625 1630

Pro Thr His Met Lys Ala Ile Leu Ser Tyr Ile Asp Leu Val Arg Met
1635 1640 1645

Gly Leu Ile Asn Val Asp Lys Leu Thr Ile Lys Asn Lys Asn Lys Phe
1650 1655 1660

Asn Asp Glu Phe Tyr Thr Ser Asn Leu Phe Tyr Ile Ser Tyr Asn Phe
1665 1670 1675 1680

Ser Asp Asn Thr His Leu Leu Thr Lys Gln Ile Arg Ile Ala Asn Ser
1685 1690 1695

Glu Leu Glu Asp Asn Tyr Asn Lys Leu Tyr His Pro Thr Pro Glu Thr
1700 1705 1710

Leu Glu Asn Met Ser Leu Ile Pro Val Lys Ser Asn Asn Ser Asn Lys
1715 1720 1725

Pro Lys Phe Cys Ile Ser Gly Asn Thr Glu Ser Met Met Met Ser Thr
1730 1735 1740

Phe Ser Ser Lys Met His Ile Lys Ser Ser Thr Val Thr Thr Arg Phe
1745 1750 1755 1760

Asn Tyr Ser Lys Gln Asp Leu Tyr Asn Leu Phe Pro Ile Val Val Ile
1765 1770 1775

Asp Lys Ile Ile Asp His Ser Gly Asn Thr Ala Lys Ser Asn Gln Leu
1780 1785 1790

Tyr Thr Thr Thr Ser His Gln Thr Ser Leu Val Arg Asn Ser Ala Ser
1795 1800 1805

Leu Tyr Cys Met Leu Pro Trp His His Val Asn Arg Phe Asn Phe Val
1810 1815 1820

Phe Ser Ser Thr Gly Cys Lys Ile Ser Ile Glu Tyr Ile Leu Lys Asp
1825 1830 1835 1840

Leu Lys Ile Lys Asp Pro Ser Cys Ile Ala Phe Ile Gly Glu Gly Ala
1845 1850 1855

Gly Asn Leu Leu Leu Arg Thr Val Val Glu Leu His Pro Asp Ile Arg
1860 1865 1870

Tyr Ile Tyr Arg Ser Leu Lys Asp Cys Asn Asp His Ser Leu Pro Ile
1875 1880 1885

Glu Phe Leu Arg Leu Tyr Asn Gly His Ile Asn Ile Asp Tyr Gly Glu
1890 1895 1900

Asn Leu Thr Ile Pro Ala Thr Asp Ala Thr Asn Asn Ile His Trp Ser

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1905                1910                1915                1920

Tyr Leu His Ile Lys Phe Ala Glu Pro Ile Ser Ile Phe Val Cys Asp
                1925                1930                1935

Ala Glu Leu Pro Val Thr Ala Asn Trp Ser Lys Ile Ile Ile Glu Trp
            1940                1945                1950

Ser Lys His Val Arg Lys Cys Lys Tyr Cys Ser Ser Val Asn Arg Cys
        1955                1960                1965

Ile Leu Ile Ala Lys Tyr His Ala Gln Asp Asp Ile Asp Phe Lys Leu
    1970                1975                1980

Asp Asn Ile Thr Ile Leu Lys Thr Tyr Val Cys Leu Gly Ser Lys Leu
1985                1990                1995                2000

Lys Gly Ser Glu Val Tyr Leu Ile Leu Thr Ile Gly Pro Ala Asn Ile
                2005                2010                2015

Leu Pro Val Phe Asp Val Val Gln Asn Ala Lys Leu Ile Leu Ser Arg
            2020                2025                2030

Thr Lys Asn Phe Ile Met Pro Lys Lys Thr Asp Lys Glu Ser Ile Asp
        2035                2040                2045

Ala Asn Ile Lys Ser Leu Ile Pro Phe Leu Cys Tyr Pro Ile Thr Lys
    2050                2055                2060

Lys Gly Ile Lys Thr Ser Leu Ser Lys Leu Lys Ser Val Val Asn Gly
2065                2070                2075                2080

Asp Ile Leu Ser Tyr Ser Ile Ala Gly Arg Asn Glu Val Phe Ser Asn
                2085                2090                2095

Lys Leu Ile Asn His Lys His Met Asn Ile Leu Lys Trp Leu Asp His
            2100                2105                2110

Val Leu Asn Phe Arg Ser Ala Glu Leu Asn Tyr Asn His Leu Tyr Met
        2115                2120                2125

Ile Glu Ser Thr Tyr Pro Tyr Leu Ser Glu Leu Leu Asn Ser Leu Thr
    2130                2135                2140

Thr Asn Glu Leu Lys Lys Leu Ile Lys Ile Thr Gly Ser Val Leu Tyr
2145                2150                2155                2160

Asn Leu Pro Asn Glu Gln
                2165
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(2) INFORMATION FOR SEQ ID NO:33:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 15219 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:33:

ACGGGAAAAA AATGCGTACT ACAAACTTGC ACATTCGAAA AAAATGGGGC AAATAAGAAC 60

TTGATAAGTG CTATTTAAGT CTAACCTTTT CAATCAGAAA TGGGGTGCAA TTCACTGAGC 120

ATGATAAAGG TTAGATTACA AAATTTATTT GACAATGACG AAGTAGCATT GTTAAAAATA 180

ACATGTTATA CTGATAAATT AATTCTTCTG ACCAATGCAT TAGCCAAAGC AGCAATACAT 240

ACAATTAAAT TAAACGGCAT AGTTTTTATA CATGTTATAA CAAGCAGTGA AGTGTGCCCT 300

GATAACAATA TTGTAGTGAA ATCTAACTTT ACAACAATGC CAATACTACA AAATGGAGGA 360

TACATATGGG AATTGATTGA GTTGACACAC TGCTCTCAAT TAAACGGTTT AATGGATGAT 420

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ACACAACGAG ACATTAGTTT TTGACACTTT TTTTCTCGT 15219

(2) INFORMATION FOR SEQ ID NO:34:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 2166 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:34:

```
Met Asp Pro Ile Ile Asn Gly Asn Ser Ala Asn Val Tyr Leu Thr Asp
1               5                   10                  15

Ser Tyr Leu Lys Gly Val Ile Ser Phe Ser Glu Cys Asn Ala Leu Gly
            20                  25                  30

Ser Tyr Leu Phe Asn Gly Pro Tyr Leu Lys Asn Asp Tyr Thr Asn Leu
        35                  40                  45

Ile Ser Arg Gln Ser Pro Leu Leu Glu His Met Asn Leu Lys Lys Leu
    50                  55                  60

Thr Ile Thr Gln Ser Leu Ile Ser Arg Tyr His Lys Gly Glu Leu Lys
65                  70                  75                  80

Leu Glu Glu Pro Thr Tyr Phe Gln Ser Leu Leu Met Thr Tyr Lys Ser
                85                  90                  95

Met Ser Ser Ser Glu Gln Ile Ala Thr Thr Asn Leu Leu Lys Lys Ile
            100                 105                 110

Ile Arg Arg Ala Ile Glu Ile Ser Asp Val Lys Val Tyr Ala Ile Leu
        115                 120                 125

Asn Lys Leu Gly Leu Lys Glu Lys Asp Arg Val Lys Pro Asn Asn Asn
    130                 135                 140

Ser Gly Asp Glu Asn Ser Val Leu Thr Thr Ile Ile Lys Asp Asp Ile
145                 150                 155                 160

Leu Ser Ala Val Glu Asn Asn Gln Ser Tyr Thr Asn Ser Asp Lys Ser
                165                 170                 175

His Ser Val Asn Gln Asn Ile Thr Ile Lys Thr Thr Leu Leu Lys Lys
            180                 185                 190
```

Leu Met Cys Ser Met Gln His Pro Pro Ser Trp Leu Ile His Trp Phe
195 200 205

Asn Leu Tyr Thr Lys Leu Asn Asn Ile Leu Thr Gln Tyr Arg Ser Asn
210 215 220

Glu Val Lys Ser His Gly Phe Ile Leu Ile Asp Asn Gln Thr Leu Ser
225 230 235 240

Gly Phe Gln Phe Ile Leu Asn Gln Tyr Gly Cys Ile Val Tyr His Lys
245 250 255

Gly Leu Lys Lys Ile Thr Thr Thr Thr Tyr Asn Gln Phe Leu Thr Trp
260 265 270

Lys Asp Ile Ser Leu Ser Arg Leu Asn Val Cys Leu Ile Thr Trp Ile
275 280 285

Ser Asn Cys Leu Asn Thr Leu Asn Lys Ser Leu Gly Leu Arg Cys Gly
290 295 300

Phe Asn Asn Val Val Leu Ser Gln Leu Phe Leu Tyr Gly Asp Cys Ile
305 310 315 320

Leu Lys Leu Phe His Asn Glu Gly Phe Tyr Ile Ile Lys Glu Val Glu
325 330 335

Gly Phe Ile Met Ser Leu Ile Leu Asn Ile Thr Glu Glu Asp Gln Phe
340 345 350

Arg Lys Arg Phe Tyr Asn Ser Met Leu Asn Asn Ile Thr Asp Ala Ala
355 360 365

Ile Lys Ala Gln Lys Asp Leu Leu Ser Arg Val Cys His Thr Leu Leu
370 375 380

Asp Lys Thr Val Ser Asp Asn Ile Ile Asn Gly Lys Trp Ile Ile Leu
385 390 395 400

Leu Ser Lys Phe Leu Lys Leu Ile Lys Leu Ala Gly Asp Asn Asn Leu
405 410 415

Asn Asn Leu Ser Glu Leu Tyr Phe Leu Phe Arg Ile Phe Gly His Pro
420 425 430

Met Val Asp Glu Arg Gln Ala Met Asp Ser Val Arg Ile Asn Cys Asn
435 440 445

Glu Thr Lys Phe Tyr Leu Leu Ser Ser Leu Ser Thr Leu Arg Gly Ala
450 455 460

Phe Ile Tyr Arg Ile Ile Lys Gly Phe Val Asn Thr Tyr Asn Arg Trp

465 470 475 480

Pro Thr Leu Arg Asn Ala Ile Val Leu Pro Leu Arg Trp Leu Asn Tyr
485 490 495

Tyr Lys Leu Asn Thr Tyr Pro Ser Leu Leu Glu Ile Thr Glu Asn Asp
500 505 510

Leu Ile Ile Leu Ser Gly Leu Arg Phe Tyr Arg Glu Phe His Leu Pro
515 520 525

Lys Lys Val Asp Leu Glu Met Ile Ile Asn Asp Lys Ala Ile Ser Pro
530 535 540

Pro Lys Asp Leu Ile Trp Thr Ser Phe Pro Arg Asn Tyr Met Pro Ser
545 550 555 560

His Ile Gln Asn Tyr Ile Glu His Glu Lys Leu Lys Phe Ser Glu Ser
565 570 575

Asp Arg Ser Arg Arg Val Leu Glu Tyr Tyr Leu Arg Asp Asn Lys Phe
580 585 590

Asn Glu Cys Asp Leu Tyr Asn Cys Val Val Asn Gln Ser Tyr Leu Asn
595 600 605

Asn Ser Asn His Val Val Ser Leu Thr Gly Lys Glu Arg Glu Leu Ser
610 615 620

Val Gly Arg Met Phe Ala Met Gln Pro Gly Met Phe Arg Gln Ile Gln
625 630 635 640

Ile Leu Ala Glu Lys Met Ile Ala Glu Asn Ile Leu Gln Phe Phe Pro
645 650 655

Glu Ser Leu Thr Arg Tyr Gly Asp Leu Glu Leu Gln Lys Ile Leu Glu
660 665 670

Leu Lys Ala Gly Ile Ser Asn Lys Ser Asn Arg Tyr Asn Asp Asn Tyr
675 680 685

Asn Asn Tyr Ile Ser Lys Cys Ser Ile Ile Thr Asp Leu Ser Lys Phe
690 695 700

Asn Gln Ala Phe Arg Tyr Glu Thr Ser Cys Ile Cys Ser Asp Val Leu
705 710 715 720

Asp Glu Leu His Gly Val Gln Ser Leu Phe Ser Trp Leu His Leu Thr
725 730 735

Ile Pro Leu Val Thr Ile Ile Cys Thr Tyr Arg His Ala Pro Pro Phe
740 745 750

Ile Lys Asp His Val Val Asn Leu Asn Glu Val Asp Glu Gln Ser Gly
755 760 765

Leu Tyr Arg Tyr His Met Gly Gly Ile Glu Gly Trp Cys Gln Lys Leu
770 775 780

Trp Thr Ile Glu Ala Ile Ser Leu Leu Asp Leu Ile Ser Leu Lys Gly
785 790 795 800

Lys Phe Ser Ile Thr Ala Leu Ile Asn Gly Asp Asn Gln Ser Ile Asp
805 810 815

Ile Ser Lys Pro Val Arg Leu Ile Glu Gly Gln Thr His Ala Gln Ala
820 825 830

Asp Tyr Leu Leu Ala Leu Asn Ser Leu Lys Leu Leu Tyr Lys Glu Tyr
835 840 845

Ala Gly Ile Gly His Lys Leu Lys Gly Thr Glu Thr Tyr Ile Ser Arg
850 855 860

Asp Met Gln Phe Met Ser Lys Thr Ile Gln His Asn Gly Val Tyr Tyr
865 870 875 880

Pro Ala Ser Ile Lys Lys Val Leu Arg Val Gly Pro Trp Ile Asn Thr
885 890 895

Ile Leu Asp Asp Phe Lys Val Ser Leu Glu Ser Ile Gly Ser Leu Thr
900 905 910

Gln Glu Leu Glu Tyr Arg Gly Glu Ser Leu Leu Cys Ser Leu Ile Phe
915 920 925

Arg Asn Ile Trp Leu Tyr Asn Gln Ile Ala Leu Gln Leu Arg Asn His
930 935 940

Ala Leu Cys Asn Asn Lys Leu Tyr Leu Asp Ile Leu Lys Val Leu Lys
945 950 955 960

His Leu Lys Thr Phe Phe Asn Leu Asp Ser Ile Asp Met Ala Leu Ser
965 970 975

Leu Tyr Met Asn Leu Pro Met Leu Phe Gly Gly Gly Asp Pro Asn Leu
980 985 990

Leu Tyr Arg Ser Phe Tyr Arg Arg Thr Pro Asp Phe Leu Thr Glu Ala
995 1000 1005

Ile Val His Ser Val Phe Val Leu Ser Tyr Tyr Thr Gly His Asp Leu
1010 1015 1020

Gln Asp Lys Leu Gln Asp Leu Pro Asp Asp Arg Leu Asn Lys Phe Leu
1025 1030 1035 1040

Thr Cys Val Ile Thr Phe Asp Lys Asn Pro Asn Ala Glu Phe Val Thr
1045 1050 1055

Leu Met Arg Asp Pro Gln Ala Leu Gly Ser Glu Arg Gln Ala Lys Ile
1060 1065 1070

Thr Ser Glu Ile Asn Arg Leu Ala Val Thr Glu Val Leu Ser Ile Ala
1075 1080 1085

Pro Asn Lys Ile Phe Ser Lys Ser Ala Gln His Tyr Thr Thr Thr Glu
1090 1095 1100

Ile Asp Leu Asn Asp Ile Met Gln Asn Ile Glu Pro Thr Tyr Pro His
1105 1110 1115 1120

Gly Leu Arg Val Val Tyr Glu Ser Leu Pro Phe Tyr Lys Ala Glu Lys
1125 1130 1135

Ile Val Asn Leu Ile Ser Gly Thr Lys Ser Ile Thr Asn Ile Leu Glu
1140 1145 1150

Lys Thr Ser Ala Ile Asp Thr Thr Asp Ile Asn Arg Ala Thr Asp Met
1155 1160 1165

Met Arg Lys Asn Ile Thr Leu Leu Ile Arg Ile Leu Pro Leu Asp Cys
1170 1175 1180

Asn Lys Asp Lys Arg Glu Leu Leu Ser Leu Glu Asn Leu Ser Ile Thr
1185 1190 1195 1200

Glu Leu Ser Lys Tyr Val Arg Glu Arg Ser Trp Ser Leu Ser Asn Ile
1205 1210 1215

Val Gly Val Thr Ser Pro Ser Ile Met Phe Thr Met Asp Ile Lys Tyr
1220 1225 1230

Thr Thr Ser Thr Ile Ala Ser Gly Ile Ile Ile Glu Lys Tyr Asn Val
1235 1240 1245

Asn Ser Leu Thr Arg Gly Glu Arg Gly Pro Thr Lys Pro Trp Val Gly
1250 1255 1260

Ser Ser Thr Gln Glu Lys Lys Thr Met Pro Val Tyr Asn Arg Gln Val
1265 1270 1275 1280

Leu Thr Lys Lys Gln Arg Asp Gln Ile Asp Leu Leu Ala Lys Leu Asp
1285 1290 1295

Trp Val Tyr Ala Ser Ile Asp Asn Lys Asp Glu Phe Met Glu Glu Leu

1300 1305 1310

Ser Thr Gly Thr Leu Gly Leu Ser Tyr Glu Lys Ala Lys Lys Leu Phe
1315 1320 1325

Pro Gln Tyr Leu Ser Val Asn Tyr Leu His Arg Leu Thr Val Ser Ser
1330 1335 1340

Arg Pro Cys Glu Phe Pro Ala Ser Ile Pro Ala Tyr Arg Thr Thr Asn
1345 1350 1355 1360

Tyr His Phe Asp Thr Ser Pro Ile Asn His Val Leu Thr Glu Lys Tyr
1365 1370 1375

Gly Asp Glu Asp Ile Asp Ile Val Phe Gln Asn Cys Ile Ser Phe Gly
1380 1385 1390

Leu Ser Leu Met Ser Val Val Glu Gln Phe Thr Asn Ile Cys Pro Asn
1395 1400 1405

Arg Ile Ile Leu Ile Pro Lys Leu Asn Glu Ile His Leu Met Lys Pro
1410 1415 1420

Pro Ile Phe Thr Gly Asp Val Asp Ile Ile Lys Leu Lys Gln Val Ile
1425 1430 1435 1440

Gln Lys Gln His Met Phe Leu Pro Asp Lys Ile Ser Leu Thr Gln Tyr
1445 1450 1455

Val Glu Leu Phe Leu Ser Asn Lys Ala Leu Lys Ser Gly Ser His Ile
1460 1465 1470

Asn Ser Asn Leu Ile Leu Val His Lys Met Ser Asp Tyr Phe His Asn
1475 1480 1485

Ala Tyr Ile Leu Ser Thr Asn Leu Ala Gly His Trp Ile Leu Ile Ile
1490 1495 1500

Gln Leu Met Lys Asp Ser Lys Gly Ile Phe Glu Lys Asp Trp Gly Glu
1505 1510 1515 1520

Gly Tyr Ile Thr Asp His Met Phe Ile Asn Leu Asn Val Phe Phe Asn
1525 1530 1535

Ala Tyr Lys Thr Tyr Leu Leu Cys Phe His Lys Gly Tyr Gly Lys Ala
1540 1545 1550

Lys Leu Glu Cys Asp Met Asn Thr Ser Asp Leu Leu Cys Val Leu Glu
1555 1560 1565

Leu Ile Asp Ser Ser Tyr Trp Lys Ser Met Ser Lys Val Phe Leu Glu
1570 1575 1580

Gln Lys Val Ile Lys Tyr Ile Val Asn Gln Asp Thr Ser Leu Arg Arg
1585 1590 1595 1600

Ile Lys Gly Cys His Ser Phe Lys Leu Trp Phe Leu Lys Arg Leu Asp
1605 1610 1615

Asn Ala Lys Phe Thr Val Cys Pro Trp Val Val Asn Ile Asp Tyr His
1620 1625 1630

Pro Thr His Met Lys Ala Ile Leu Ser Tyr Ile Asp Leu Val Arg Met
1635 1640 1645

Gly Leu Ile Asn Val Asp Lys Leu Thr Ile Lys Asn Lys Asn Lys Phe
1650 1655 1660

Asn Asp Glu Phe Tyr Thr Ser Asn Leu Phe Tyr Ile Ser Tyr Asn Phe
1665 1670 1675 1680

Ser Asp Asn Thr His Leu Leu Thr Lys Gln Ile Arg Ile Ala Asn Ser
1685 1690 1695

Glu Leu Glu Asp Asn Tyr Asn Lys Leu Tyr His Pro Thr Pro Glu Thr
1700 1705 1710

Leu Glu Asn Met Ser Leu Ile Pro Val Lys Ser Asn Asn Ser Asn Lys
1715 1720 1725

Pro Lys Phe Cys Ile Ser Gly Asn Thr Glu Ser Met Met Met Ser Thr
1730 1735 1740

Phe Ser Ser Lys Met His Ile Lys Ser Ser Thr Val Thr Thr Arg Phe
1745 1750 1755 1760

Asn Tyr Ser Lys Gln Asp Leu Tyr Asn Leu Phe Pro Ile Val Val Ile
1765 1770 1775

Asp Lys Ile Ile Asp His Ser Gly Asn Thr Ala Lys Ser Asn Gln Leu
1780 1785 1790

Tyr Thr Thr Thr Ser His Gln Thr Ser Leu Val Arg Asn Ser Ala Ser
1795 1800 1805

Leu Tyr Cys Met Leu Pro Trp His His Val Asn Arg Phe Asn Phe Val
1810 1815 1820

Phe Ser Ser Thr Gly Cys Lys Ile Ser Ile Glu Tyr Ile Leu Lys Asp
1825 1830 1835 1840

Leu Lys Ile Lys Asp Pro Ser Cys Ile Ala Phe Ile Gly Glu Gly Ala
1845 1850 1855

Gly Asn Leu Leu Leu Arg Thr Val Val Glu Leu His Pro Asp Ile Arg
1860 1865 1870

Tyr Ile Tyr Arg Ser Leu Lys Asp Cys Asn Asp His Ser Leu Pro Ile
1875 1880 1885

Glu Phe Leu Arg Leu Tyr Asn Gly His Ile Asn Ile Asp Tyr Gly Glu
1890 1895 1900

Asn Leu Thr Ile Pro Ala Thr Asp Ala Thr Asn Asn Ile His Trp Ser
1905 1910 1915 1920

Tyr Leu His Ile Lys Phe Ala Glu Pro Ile Ser Ile Phe Val Cys Asp
1925 1930 1935

Ala Glu Leu Pro Val Thr Ala Asn Trp Ser Lys Ile Ile Ile Glu Trp
1940 1945 1950

Ser Lys His Val Arg Lys Cys Lys Tyr Cys Ser Ser Val Asn Arg Cys
1955 1960 1965

Ile Leu Ile Ala Lys Tyr His Ala Gln Asp Asp Ile Asp Phe Lys Leu
1970 1975 1980

Asp Asn Ile Thr Ile Leu Lys Thr Tyr Val Cys Leu Gly Ser Lys Leu
1985 1990 1995 2000

Lys Gly Ser Glu Val Tyr Leu Ile Leu Thr Ile Gly Pro Ala Asn Ile
2005 2010 2015

Leu Pro Val Phe Asp Val Val Gln Asn Ala Lys Leu Ile Leu Ser Arg
2020 2025 2030

Thr Lys Asn Phe Ile Met Pro Lys Lys Thr Asp Lys Glu Ser Ile Asp
2035 2040 2045

Ala Val Ile Lys Ser Leu Ile Pro Phe Leu Cys Tyr Pro Ile Thr Lys
2050 2055 2060

Lys Gly Ile Lys Thr Ser Leu Ser Lys Leu Lys Ser Val Val Asn Gly
2065 2070 2075 2080

Asp Ile Leu Ser Tyr Ser Ile Ala Gly Arg Asn Glu Val Phe Ser Asn
2085 2090 2095

Lys Leu Ile Asn His Lys His Met Asn Ile Leu Lys Trp Leu Asp His
2100 2105 2110

Val Leu Asn Phe Arg Ser Ala Glu Leu Asn Tyr Asn His Leu Tyr Met
2115 2120 2125

Ile Glu Ser Thr Tyr Pro Tyr Leu Ser Glu Leu Leu Asn Ser Leu Thr

2130 2135 2140

Thr Asn Glu Leu Lys Lys Leu Ile Lys Ile Thr Gly Ser Val Leu Tyr
2145 2150 2155 2160

Asn Leu Pro Asn Glu Gln
2165

(2) INFORMATION FOR SEQ ID NO:35:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:35:

CATATCACTC ACTCTGGGAT GGAG 24

(2) INFORMATION FOR SEQ ID NO:36:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:36:

TCAGAACATC AAGCACCGCC 20

(2) INFORMATION FOR SEQ ID NO:37:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:37:

ACAGTCAAGA CTGAGATGAG 20

(2) INFORMATION FOR SEQ ID NO:38:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:38:

AAGAGTCAGA TACATGTGGA 20

(2) INFORMATION FOR SEQ ID NO:39:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:39:

ACATGAATCA GCCTAAAGTC 20

(2) INFORMATION FOR SEQ ID NO:40:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 25 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:40:

CCGAAAGAGT TCCTGCGTTA CGACC 25

(2) INFORMATION FOR SEQ ID NO:41:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:41:

CAGTCCACAC AAGTACCAGG 20

(2) INFORMATION FOR SEQ ID NO:42:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:42:

GTCAGAAGCT GTGGACCATC 20

(2) INFORMATION FOR SEQ ID NO:43:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:43:

AATATTGCTA CAACAATGGC 20

(2) INFORMATION FOR SEQ ID NO:44:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:44:

ACTCTTCATT CCTAGACTGG 20

(2) INFORMATION FOR SEQ ID NO:45:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:45:

GTCCAATTAT GACTATGAAC 20

(2) INFORMATION FOR SEQ ID NO:46:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:46:

AGAACAGACA TGAAGCTTGC 20

(2) INFORMATION FOR SEQ ID NO:47:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:47:

CCAACAAGGA ATGCTTCTAG 20

(2) INFORMATION FOR SEQ ID NO:48:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 25 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:48:

ACAGCACTAT CTATGATTGA CCTGG 25

(2) INFORMATION FOR SEQ ID NO:49:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:49:

GCAACATGGT TTACACATGC 20

(2) INFORMATION FOR SEQ ID NO:50:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:50:

AGATTGAGAG TTGATCCAGG 20

(2) INFORMATION FOR SEQ ID NO:51:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:51:

AGGAGATACT TAAACTAAGC 20

(2) INFORMATION FOR SEQ ID NO:52:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:52:

TAAGCTTATG CCTTTCAGCG 20

(2) INFORMATION FOR SEQ ID NO:53:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:53:

TTAACGGACC TAAGCTGTGC 20

(2) INFORMATION FOR SEQ ID NO:54:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:54:

GAAACAGATT ATTATGACGG 20

(2) INFORMATION FOR SEQ ID NO:55:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:55:

CGGGCTATCT AGGTGAACTT CAGG 24

(2) INFORMATION FOR SEQ ID NO:56:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:56:

ATTTGGATAT GGAATATGAG 20

(2) INFORMATION FOR SEQ ID NO:57:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:57:

ACTCAACTGA ACTACCAGTG 20

(2) INFORMATION FOR SEQ ID NO:58:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:58:

AAGAACATCA TGTATTTCAG 20

(2) INFORMATION FOR SEQ ID NO:59:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:59:

TTATCAACGC ACTGCTCATG 20

(2) INFORMATION FOR SEQ ID NO:60:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 25 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:60:

ATTTTCAGCA ATCACTTGGC ATGCC 25

(2) INFORMATION FOR SEQ ID NO:61:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:61:

GCCTCTGTGC AAACAAGCTG 20

(2) INFORMATION FOR SEQ ID NO:62:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:62:

TCTCTAGTTA CTCTAGCAGC 20

(2) INFORMATION FOR SEQ ID NO:63:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:63:

AGGTCGTTGT TTGTGAGGAG 20

(2) INFORMATION FOR SEQ ID NO:64:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:64:

TCGTCCTCTT CTTTACTGTC 20

(2) INFORMATION FOR SEQ ID NO:65:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:65:

CCGTCCTCGA GCTAGCCTCG 20

(2) INFORMATION FOR SEQ ID NO:66:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:66:

CTCCTCCAGG CTCACATTGG 20

(2) INFORMATION FOR SEQ ID NO:67:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:67:

GGGTTGGTAC ATAGCTCTGC 20

(2) INFORMATION FOR SEQ ID NO:68:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 25 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:68:

CACCCATCTG ATATTTCCCT GATGG 25

(2) INFORMATION FOR SEQ ID NO:69:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:69:

TGGTTGACAG TACAAATCTG 20

(2) INFORMATION FOR SEQ ID NO:70:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:70:

CTGAAATGGG AAGATTGTGC 20

(2) INFORMATION FOR SEQ ID NO:71:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs

(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:71:

AGCAATCTAC ACTGCCTACC 20

(2) INFORMATION FOR SEQ ID NO:72:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:72:

TCACAGATGA TTCAATTATC 20

(2) INFORMATION FOR SEQ ID NO:73:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:73:

GATCCTAGAT ATAAGTTCTC 20

(2) INFORMATION FOR SEQ ID NO:74:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid

(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:74:

ACCAAACAAA GTTGGGTAAG G 21

(2) INFORMATION FOR SEQ ID NO:75:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 32 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:75:

GGGGGATCCA TCCCTAATCC TGCTCTTGTC CC 32

(2) INFORMATION FOR SEQ ID NO:76:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:76:

GATTCCTCTG ATGGCTCCAC 20

(2) INFORMATION FOR SEQ ID NO:77:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:77:

TAACAGTCAA GGAGACCAAA G 21

(2) INFORMATION FOR SEQ ID NO:78:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 32 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:78:

GGGAAGCTTA ACCCTAATCC TGCCCTAGGT GG 32

(2) INFORMATION FOR SEQ ID NO:79:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: RNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:79:

ACCAGACAAA GCTGGGAATA GA 22

What is claimed is:

1. An isolated, recombinantly-generated, attenuated, nonsegmented, negative-sense, single stranded RNA virus of the Order Mononegavirales having at least one attenuating mutation in the 3' genomic promoter region and having at least one attenuating mutation in the RNA polymerase gene.

2. The virus of Claim 1 wherein the virus is from the Family Paramyxoviridae.

3. The virus of Claim 2 wherein the virus is from the Subfamily Paramyxovirinae.

4. The virus of Claim 3 wherein the virus is from the Genus *Morbillivirus*.

5. The virus of Claim 4 wherein the virus is measles virus.

6. The measles virus of Claim 5 wherein:

(a) the at least one attenuating mutation in the 3' genomic promoter region is selected from the group consisting of nucleotide 26 (A $\rightarrow$ T), nucleotide 42 (A $\rightarrow$ T or A $\rightarrow$ C) and nucleotide 96 (G $\rightarrow$ A), where these nucleotides are presented in positive strand, antigenomic, message sense; and

(b) the at least one attenuating mutation in the RNA polymerase gene is selected from the group consisting of nucleotide changes which produce changes in an amino acid selected from the group consisting of residues 331 (isoleucine $\rightarrow$ threonine), 1409 (alanine $\rightarrow$ threonine), 1624 (threonine $\rightarrow$ alanine), 1649 (arginine $\rightarrow$ methionine), 1717

(aspartic acid → alanine), 1936 (histidine → tyrosine), 2074 (glutamine → arginine) and 2114 (arginine → lysine).

7. The virus of Claim 3 wherein the virus is from the Genus *Paramyxovirus*.

8. The virus of Claim 7 wherein the virus is human parainfluenzae virus type 3 (PIV-3).

9. The PIV-3 of Claim 8 wherein:

(a) the at least one attenuating mutation in the 3' genomic promoter region is selected from the group consisting of nucleotide 23 (T → C), nucleotide 24 (C → T), nucleotide 28 (G → T) and nucleotide 45 (T → A), where these nucleotides are presented in positive strand, antigenomic, message sense; and

(b) the at least one attenuating mutation in the RNA polymerase gene is selected from the group consisting of nucleotide changes which produce changes in an amino acid selected from the group consisting of residues 942 (tyrosine → histidine), 992 (leucine → phenylalanine), 1292 (leucine → phenylalanine), and 1558 (threonine → isoleucine).

10. The virus of Claim 3 wherein the virus is from the Genus *Rubulavirus*.

11. The virus of Claim 2 wherein the virus is from the Subfamily Pneumovirinae.

12. The virus of Claim 11 wherein the virus is from the Genus *Pneumovirus*.

13. The virus of Claim 12 wherein the virus is human respiratory syncytial virus (RSV) subgroup B.

14. The virus of Claim 13 wherein:

(a) the at least one attenuating mutation in the 3' genomic promoter region is selected from the group consisting of nucleotide 4 (C $\rightarrow$ G) and the insertion of an additional A in the stretch of A's at nucleotides 6-11, where these nucleotides are presented in positive strand, antigenomic, message sense; and

(b) the at least one attenuating mutation in the RNA polymerase gene is selected from the group consisting of nucleotide changes which produce changes in an amino acid selected from the group consisting of residues 353 (arginine $\rightarrow$ lysine), 451 (lysine $\rightarrow$ arginine), 1229 (aspartic acid $\rightarrow$ asparagine), 2029 (threonine $\rightarrow$ isoleucine) and 2050 (asparagine $\rightarrow$ aspartic acid).

15. The virus of Claim 1 wherein the virus is from the Family Rhabdoviridae.

16. The virus of Claim 1 wherein the virus is from the Family Filoviridae.

17. A vaccine comprising an isolated, recombinantly-generated, attenuated, nonsegmented, negative-sense, single stranded RNA virus of the Order Mononegavirales according to Claim 1 and a physiologically acceptable carrier.

18. The vaccine of Claim 17 comprising a measles virus according to Claim 5 and a physiologically acceptable carrier.

19. The vaccine of Claim 18 comprising a measles virus according to Claim 6 and a physiologically acceptable carrier.

20. The vaccine of Claim 17 comprising a PIV-3 according to Claim 8 and a physiologically acceptable carrier.

21. The vaccine of Claim 20 comprising a PIV-3 according to Claim 9 and a physiologically acceptable carrier.

22. The vaccine of Claim 17 comprising an RSV subgroup B according to Claim 13 and a physiologically acceptable carrier.

23. The vaccine of Claim 22 comprising an RSV subgroup B according to Claim 14 and a physiologically acceptable carrier.

24. A method for immunizing an individual to induce protection against a nonsegmented, negative-sense, single stranded RNA virus of the Order Mononegavirales which comprises administering to the individual the vaccine of Claim 17.

25. The method of Claim 24 wherein the vaccine is the vaccine of Claim 18.

26. The method of Claim 25 wherein the vaccine is the vaccine of Claim 19.

27. The method of Claim 24 wherein the vaccine is the vaccine of Claim 20.

28. The method of Claim 27 wherein the vaccine is the vaccine of Claim 21.

29. The method of Claim 24 wherein the vaccine is the vaccine of Claim 22.

30. The method of Claim 29 wherein the vaccine is the vaccine of Claim 23.

31. An isolated nucleic acid molecule comprising a measles virus sequence in positive strand, antigenomic message sense selected from the group consisting of 1977 wild-type strain (SEQ ID NO:3), 1983 wild-type strain (SEQ ID NO:5) where the nucleotide 2499 is G or C, Montefiore wild-type strain (SEQ ID NO:7), Rubeovax™ vaccine strain (SEQ ID NO:9), where the nucleotide 2143 is T or C, Moraten vaccine strain (SEQ ID NO:11), Schwarz vaccine strain (SEQ ID NO:11), where the nucleotide 4917 is C and the nucleotide 4924 is C, and Zagreb vaccine strain (SEQ ID NO:13), and the complementary genomic sequences thereof.

32. An isolated nucleic acid molecule comprising a PIV-3 sequence in positive strand, antigenomic message sense selected from the group consisting of cp45 vaccine strain grown in fetal rhesus lung cells (SEQ ID NO:19) and cp45 vaccine strain grown in Vero cells (SEQ ID NO:21), and the complementary genomic sequences thereof.

33. A composition which comprises a transcription vector comprising an isolated nucleic acid molecule encoding a genome or antigenome of a nonsegmented, negative-sense, single stranded RNA virus of the Order Mononegavirales having at least one attenuating mutation in the 3' genomic promoter region and having at least one attenuating mutation in the RNA polymerase gene, together with at least one expression vector which comprises at least one isolated nucleic acid molecule encoding the trans-acting proteins necessary for encapsidation, transcription and replication, whereby upon expression an infectious attenuated virus is produced.

34. The composition of Claim 33 wherein the transcription vector comprises an isolated nucleic acid molecule which encodes a measles virus according to Claim 5 and the at least one expression vector comprises at least one isolated nucleic acid molecule encoding the trans-acting proteins N, P and L.

35. The composition of Claim 34 wherein the transcription vector comprises an isolated nucleic acid molecule which encodes a measles virus according to Claim 6.

36. The composition of Claim 33 wherein the transcription vector comprises an isolated nucleic acid molecule which encodes a PIV-3 according to Claim 8 and the at least one expression vector comprises at least one isolated nucleic acid molecule encoding the trans-acting proteins NP, P and L.

37. The composition of Claim 36 wherein the transcription vector comprises an isolated nucleic acid molecule which encodes a PIV-3 according to Claim 9.

38. The composition of Claim 33 wherein the transcription vector comprises an isolated nucleic acid molecule which encodes an RSV subgroup B according to Claim 13 and the at least one expression vector comprises at least one isolated nucleic acid molecule encoding the trans-acting proteins N, P, L and M2.

39. The composition of Claim 38 wherein the transcription vector comprises an isolated nucleic acid molecule which encodes an RSV subgroup B according to Claim 14.

40. A method for producing infectious attenuated nonsegmented, negative-sense, single stranded RNA virus of the Order Mononegavirales which comprises transforming or transfecting host cells with

the at least two vectors of Claim 33 and culturing the host cells under conditions which permit the co-expression of these vectors so as to produce the infectious attenuated virus.

41. The method of Claim 40 wherein the virus is the measles virus of Claim 5.

42. The method of Claim 41 wherein the virus is the measles virus of Claim 6.

43. The method of Claim 40 wherein the virus is the PIV-3 of Claim 8.

44. The method of Claim 43 wherein the virus is the PIV-3 of Claim 9.

45. The method of Claim 40 wherein the virus is the RSV subgroup B of Claim 13.

46. The method of Claim 45 wherein the virus is the RSV subgroup B of Claim 14.

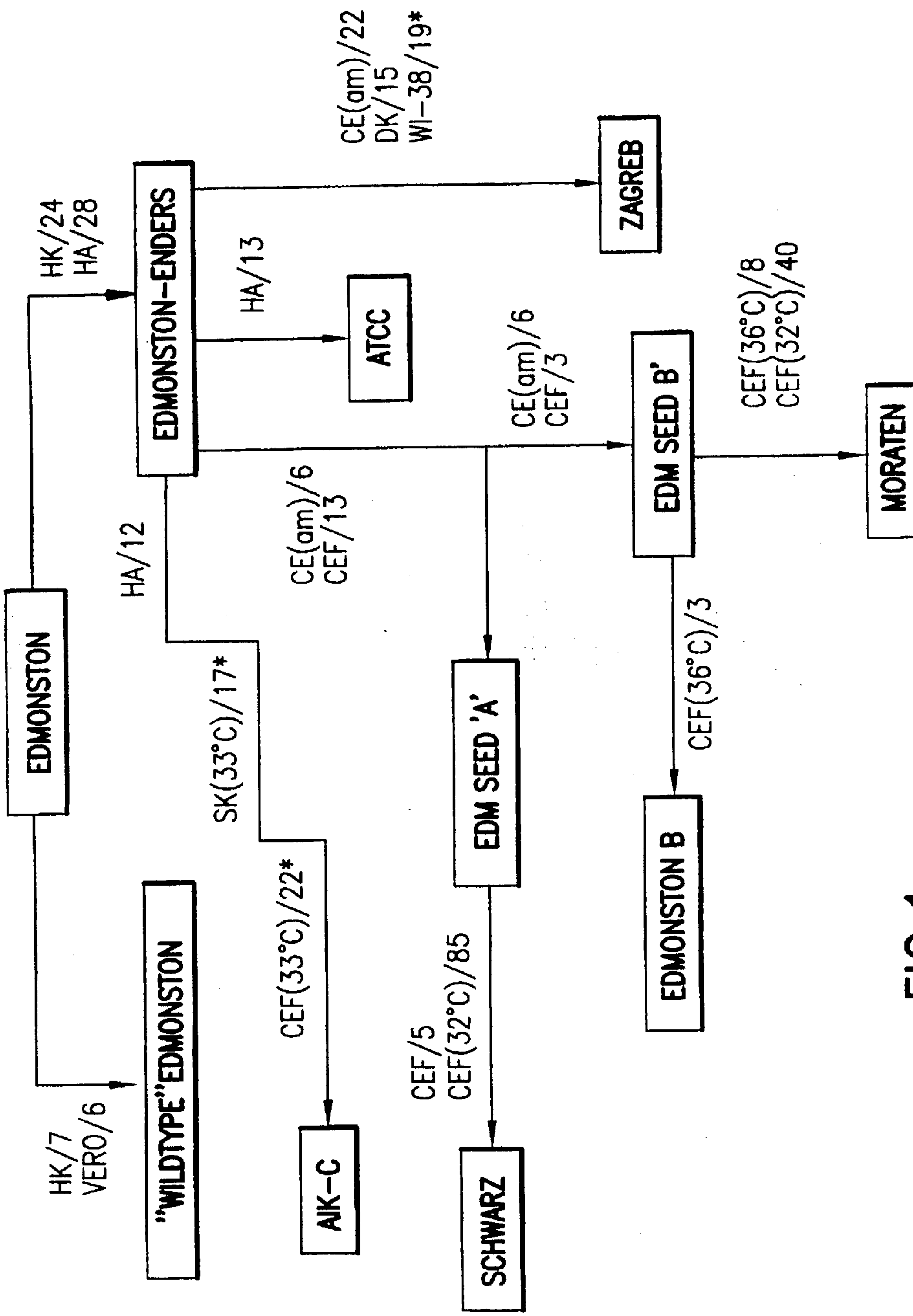
EDMONSTON
HK/24
HA/28
EDMONSTON-ENDERS
HK/7
VERO/6
"WILDTYPE" EDMONSTON
HA/12
SK(33°C)/17*
CEF(33°C)/22*
AIK-C
HA/13
ATCC
CE(am)/22
DK/15
WI-38/19*
ZAGREB
CE(am)/6
CEF/13
EDM SEED 'A'
CEF/5
CEF(32°C)/85
SCHWARZ
CE(am)/6
CEF/3
EDM SEED 'B'
CEF(36°C)/8
CEF(32°C)/40
MORATEN
CEF(36°C)/3
EDMONSTON B

FIG.1

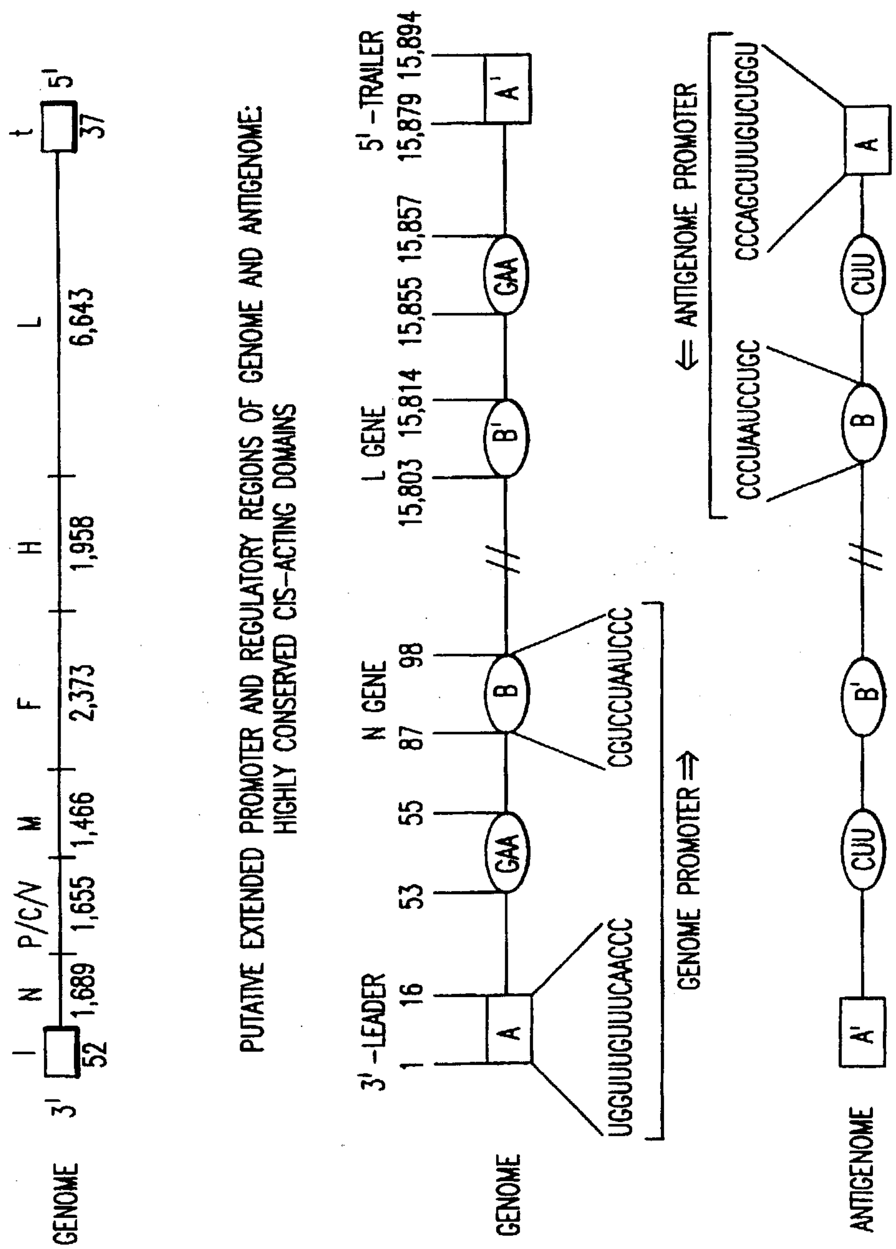
GENOME
3'
l
N
P/C/V
M
F
H
L
t
5'
52
1,689
1,655
1,466
2,373
1,958
6,643
37
PUTATIVE EXTENDED PROMOTER AND REGULATORY REGIONS OF GENOME AND ANTIGENOME:
HIGHLY CONSERVED CIS-ACTING DOMAINS
3'-LEADER
N GENE
L GENE
5'-TRAILER
1
16
53
55
87
98
15,803
15,814
15,855
15,857
15,879
15,894
GENOME
A
GAA
B
B'
GAA
A'
UGGUUUGUUUCAACCC
CGUCCUAAUCCC
GENOME PROMOTER ⇒
⇐ ANTIGENOME PROMOTER
CCCUAAUCCUGC
CCCAGCUUUGUCUGGU
ANTIGENOME
A'
CUU
B'
B
CUU
A

FIG.2

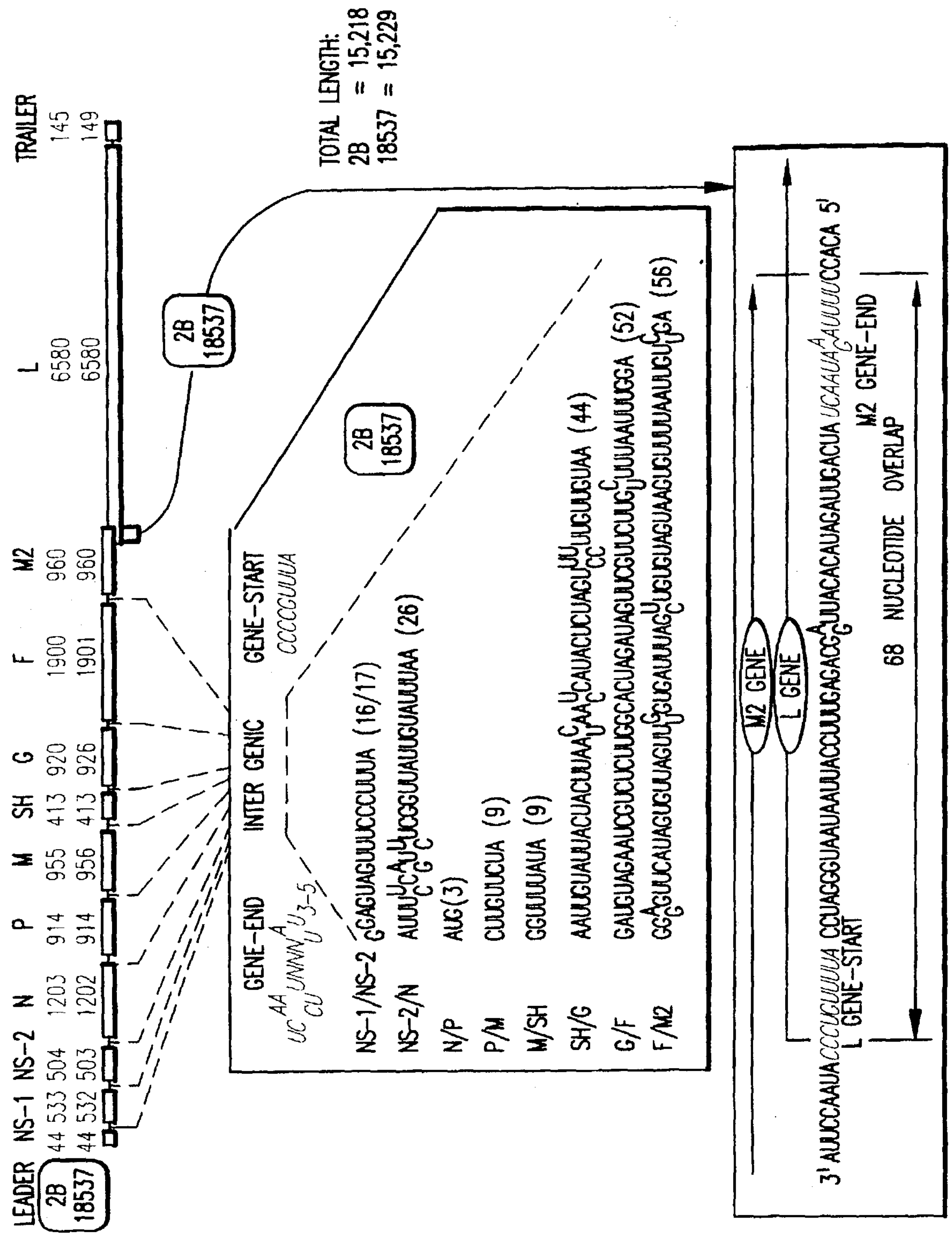
LEADER
2B
18537
NS-1 NS-2 N P M SH G F M2 L TRAILER
44 533 504 1203 914 955 413 920 1900 960 6580 145
44 532 503 1202 914 956 413 926 1901 960 6580 149
TOTAL LENGTH:
2B = 15,218
18537 = 15,229
GENE-END INTER GENIC GENE-START
CCCCGUUUA
NS-1/NS-2 GAGUAGUUUCCCUUUA (16/17)
NS-2/N AUUUUCGGUUAUUGUAUUUAA (26)
N/P AUG(3)
P/M CUUGUUCUA (9)
M/SH GGUUUUAUA (9)
SH/G (44)
G/F (52)
F/M2 (56)
M2 GENE
L GENE
3' AUUCCAAUACCCUCUUUUA CCUAGGUAAUAAUUACCUUUGAGACGUUACACAUAGAUUGACUA UCAAUAGAUUUUCCACA 5'
L GENE-START
M2 GENE-END
68 NUCLEOTIDE OVERLAP

FIG.3

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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 :
C12N 15/45, 15/47, 15/40, C07K 14/12, 14/115, 14/135, C12N 7/04, A61K 39/165, 39/155, C07K 14/145, 14/08

A3

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(74) Agents: GORDON, Alan, M. et al.; American Home Products Corporation, Patent Law Dept. – 2B, One Campus Drive, Parsippany, NJ 07054 (US).

(81) Designated States: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, ZW, European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(88) Date of publication of the international search report: 13 August 1998 (13.08.98)

(54) Title: 3' GENOMIC PROMOTER REGION AND POLYMERASE GENE MUTATIONS RESPONSIBLE FOR ATTENUATION IN VIRUSES OF THE ORDER DESIGNATED MONONEGAVIRALES

(57) Abstract

Isolated, recombinantly–generated, attenuated, nonsegmented, negative–sense, single stranded RNA viruses of the Order Mononegavirales having at least one attenuating mutation in the 3' genomic promoter region and having at least one attenuating mutation in the RNA polymerase gene are described. Vaccines are formulated comprising such viruses and a physiologically acceptable carrier. The vaccines are used for immunizing an individual to induce protection against a nonsegmented, negative–sense, single stranded RNA virus of the Order Mononegavirales.

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INTERNATIONAL SEARCH REPORT

Interna al Application No
PCT/US 97/16718

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/45 C12N15/47 C12N15/40 C12N7/04 C07K14/12 C07K14/115 C07K14/135 A61K39/165 A61K39/155 C07K14/145 C07K14/08

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C12N C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	EP 0 702 085 A (AKZO NOBEL NV) 20 March 1996 cited in the application see the whole document ---	1-9, 17-21, 24-28, 31-37, 40-44
Y	EP 0 540 135 A (THE KITASATO INSTITUTE) 5 May 1993 see the whole document, especially SEQ.ID.1 --- -/--	1-6, 17-19, 24-26, 31, 33-35, 40-42

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
29 May 1998	29-06-1998

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Mandl, B

4

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	STOKES A. ET AL.: "The complete nucleotide sequence of two cold-adapted, temperature-sensitive attenuated mutant vaccine viruses(cp12 and cp45) derived from the JS strain of human parainfluenza virus type 3 (PIV3)." VIRUS RESEARCH, vol. 30, 1993, pages 43-52, XP002051711 cited in the application see the whole document, especially Fig. 2	1-3,7-9, 17,20, 21,24, 27,28, 32,33, 36,37, 40,43,44
A	WO 93 21306 A (THE MOUNT SINAI SCHOOL OF MEDICINE OF THE CITY UNIVERSITY OF NEW YORK) 28 October 1993 see the whole document	1-9, 11-14, 17-46
A	EP 0 440 219 A (SCHWEIZ SERUM & IMPFINST) 7 August 1991 see the whole document, especially examples	1-9, 11-14, 17-46
A	RADECKE F. ET AL.: "RESCUE OF MEASLES VIRUSES FROM CLONED DNA" EMBO JOURNAL, vol. 14, no. 23, 1 December 1995, pages 5773-5784, XP002022952 cited in the application see the whole document	1-6, 17-19, 24-26, 31, 33-35, 40-42
A	MORI T. ET AL.: "Molecular cloning and complete nucleotide sequence of genomic RNA of the AIK-C strain of attenuated measles virus." VIRUS GENES, vol. 7, no. 1, 1993, pages 67-81, XP002051752 see the whole document, especially Figure 2 and Table 3	1-6, 17-19, 24-26, 31, 33-35, 40-42
A	CROWE J.E. ET AL.: "Acquisition of the ts phenotype by a chemically mutagenized cold-passaged human respiratory syncytial virus vaccine candidate results from the acquisition of a single mutation in the polymerase (L) gene." VIRUS GENES, vol. 13, no. 3, February 1996, pages 269-273, XP002066591 see the whole document	11-14, 22,23, 29,30, 38,39, 45,46

-/--

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	COLLINS P.L. ET AL.: "Production of infectious human respiratory syncytial virus from cloned cDNA confirms an essential role for the transcription elongation factor from the 5' proximal open reading frame of the M2 mRNA in gene expression and provides a capability for vaccine development." PROC. NATL. ACAD. SCI. USA, vol. 92, December 1995, pages 11563-11567, XP002066592 cited in the application see the whole document	11-14, 22,23, 29,30, 38,39, 45,46
A	WO 93 21310 A (AMERICAN HOME PROD ;US (US)) 28 October 1993 see the whole document	11-14, 22,23, 29,30, 38,39, 45,46
A	EP 0 567 100 A (AMERICAN CYANAMID CO) 27 October 1993 see page 13, line 9 - line 53	11-14, 22,23, 29,30, 38,39, 45,46

Inte...ational application No.
PCT/US 97/16718

INTERNATIONAL SEARCH REPORT

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Remark : Although claims 25-30 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [X] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

(inventions 1,2,4) 4-9,11-14,18-23,25-32,34-39,41-46 (completely) and 1-3,17,24,33,40 (partially)

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[X] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 4-6,18,19,25,26,31,34,35,41,42 (complete) and 1-3, 17,24,33,40 (partially)

   Recombinantly generated, attenuated Morbillivirus having at least one attenuating mutation in the 3' genomic promoter region and at least one attenuating mutation in the RNA polymerase gene; vaccine comprising it; nucleic acid molecules encoding said virus; composition comprising said nucleic acid together with an expression vector providing all trans-acting proteins necessary for the production of said attenuated virus and a method of producing it.

2. Claims: 7-9,20,21,27,28,32,36,37,43,44 (complete) and 1-3, 17,24,33,40 (partially)

   Recombinantly generated, attenuated Paramyxovirus having at least one attenuating mutation in the 3' genomic promoter region and at least one attenuating mutation in the RNA polymerase gene; vaccine comprising it; nucleic acid molecules encoding said virus; composition comprising said nucleic acid together with an expression vector providing all trans-acting proteins necessary for the production of said attenuated virus and a method of producing it.

3. Claims: 10 (complete) and 1-3,17,24,33,40 (partially)

   Recombinantly generated, attenuated Rubulavirus having at least one attenuating mutation in the 3' genomic promoter region and at least one attenuating mutation in the RNA polymerase gene; vaccine comprising it; composition comprising a nucleic acid molecule encoding said virus together with an expression vector providing all trans-acting proteins necessary for the production of said attenuated virus and a method of producing it.

4. Claims: 11-14,22,23,29,30,38,39,45,46 (complete) and 1,2, 17,24,33,40 (partially)

   Recombinantly generated, attenuated Pneumovirinae having at least one attenuating mutation in the 3' genomic promoter region and at least one attenuating mutation in the RNA polymerase gene; vaccine comprising it; composition comprising a nucleic acid molecule encoding said virus together with an expression vector providing all trans-acting proteins necessary for the production of said attenuated virus and a method of producing it.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

5. Claims: 15 (complete) and 1,17,24,33,40 (partially)

Recombinantly generated, attenuated Rhabdoviridae having at least one attenuating mutation in the 3' genomic promoter region and at least one attenuating mutation in the RNA polymerase gene; vaccine comprising it; composition comprising a nucleic acid molecule encoding said virus together with an expression vector providing all trans-acting proteins necessary for the production of said attenuated virus and a method of producing it.

6. Claims: 16 (complete) and 1,17,24,33,40 (partially)

Recombinantly generated, attenuated Filoviridae having at least one attenuating mutation in the 3' genomic promoter region and at least one attenuating mutation in the RNA polymerase gene; vaccine comprising it; composition comprising a nucleic acid molecule encoding said virus together with an expression vector providing all trans-acting proteins necessary for the production of said attenuated virus and a method of producing it.

INTERNATIONAL SEARCH REPORT

Information on patent family members

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PCT/US 97/16718

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